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Imidazole series. III. Action of α-halo ketones on 2-mercaptoimidazoles. [illegible] M. Kochergin and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Sci. Research Inst., Moscow). *Zhur. Obshchei Khim.* 26, 458–66(1956); cf. *C.A.* 50, 9387*i*.—The cyclization of 4(5)-phenyl-2-β-oxoalkylmercaptoimidazoles to imidazo-[2,1-*b*]-thiazoles is catalyzed by H ions. A soln. of 1.3 g. Na, 100 ml. 96% EtOH and 10 g. 4(5)-phenyl-2-mercaptoimidazole was heated 1.2 hrs. with 7.9 g. 2-chlorocyclohexanone at 55–60° (finally at reflux) yielding 97.7% *4(5)-phenyl-2-(2-cyclohexanon-1-yl)mercaptoimidazole* (I), m. 123–4° (from EtOH). The action of appropriate halo ketones similarly yielded the following *2-β-oxoalkylmercapto-4(5)arylimidazoles* (*oxoalkyl group* and *aryl group* shown, resp.): *AcCH*$_2$, *Ph*, 94.8%, m. 120–1° (*HCl salt*, m. 153°; *semicarbazone*, m. 146–8°); *AcCHMe*, *Ph*, 86.3%, m. 96–7° (*HCl salt*, m. 220–2°; *HBr salt*, m. 226–7°; *semicarbazone*, m. 179–81); *p*-O$_2$NC$_6$H$_4$-*BzCH*$_2$, *Ph*, 98.8%, m. 135–6° (*HCl salt*, m. 220–2°; *HBr salt*, m. 226–7°; *semicarbazone*, m. 179–81); *p*-O$_2$NC$_6$H$_4$-*COCH*$_2$, *Ph*, 96.7%, m. 155°; *m*-O$_2$NC$_6$H$_4$*COCH*$_2$, *Ph*, 97.6%, m. 173–5°; *AcCH*$_2$, *p*-O$_2$NC$_6$H$_4$, 93.1%, m. 169.5–70°; *AcCHMe*, *p*-O$_2$NC$_6$H$_4$, 90%, m. 130–2°; *2-cyclohexanon-1-yl*, *p*-O$_2$NC$_6$H$_4$, 95.1%, m. 182–3°. Refluxing 5 g. 4(5)-phenyl-2-mercaptoimidazole in 80 ml. 38% HCl with 2.75 g. AcCH$_2$Cl 1 hr. gave after treatment with C and cooling 91.5% *3-methyl-6-phenylimidazo[2,1-b]thiazole HCl salt*, decomp. 228–32°, which with NaHCO$_3$ gave the *free base*, m. 113–13.5°, identical with a specimen prepd. from 4-methyl-2-aminothiazole and BzCH$_2$Br, or from refluxing 4(5)-phenyl-2-acetonylmercaptoimidazole 1 hr. in concd. HCl, or from refluxing the HCl salt of the latter in BuOH 1 hr. The same procedure yielded *2,3-dimethyl-6-phenylimidazo[2,1-b]thiazole*, m. 157–8°; *HCl salt*, m. 237–9°.

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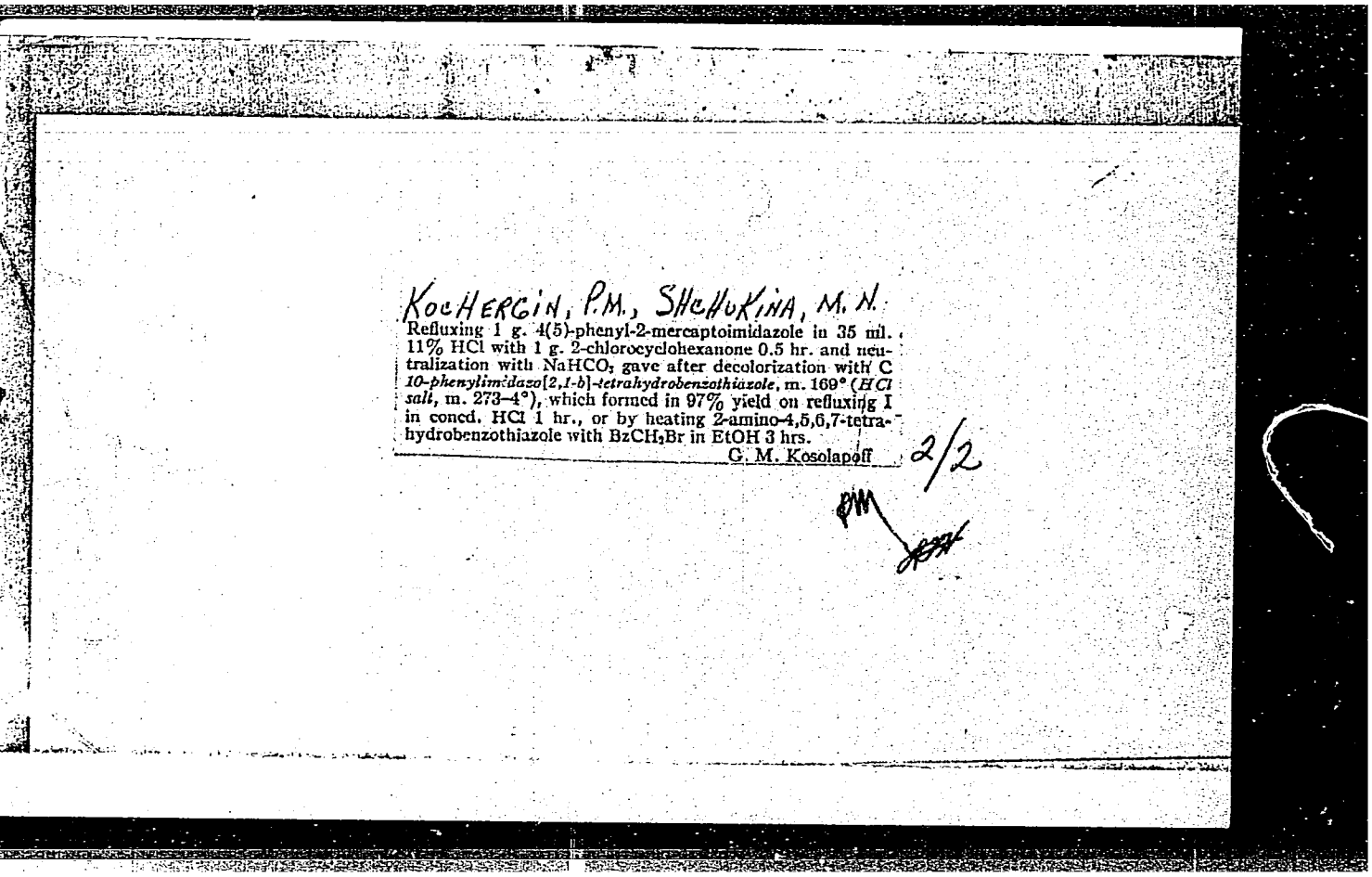

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Refluxing 1 g. 4(5)-phenyl-2-mercaptoimidazole in 35 ml. 11% HCl with 1 g. 2-chlorocyclohexanone 0.5 hr. and neutralization with $NaHCO_3$ gave after decolorization with C *10-phenylimidazo[2,1-b]-tetrahydrobenzothiazole*, m. 169° (*HCl salt*, m. 273–4°), which formed in 97% yield on refluxing I in concd. HCl 1 hr., or by heating 2-amino-4,5,6,7-tetrahydrobenzothiazole with $BzCH_2Br$ in EtOH 3 hrs.

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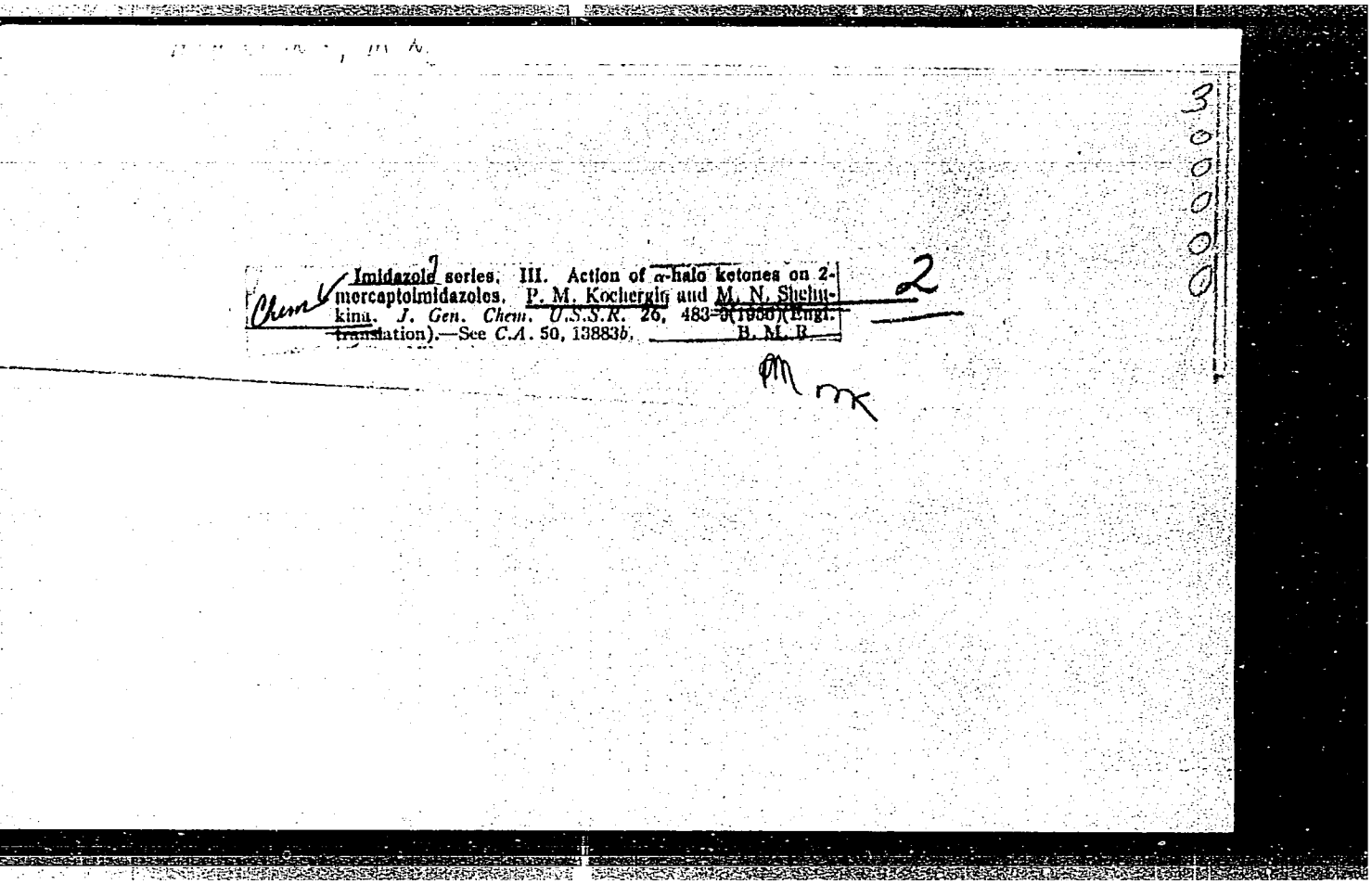

Imidazole series. III. Action of α-halo ketones on 2-mercaptoimidazoles. P. M. Kochergin and M. N. Shchukina. *J. Gen. Chem. U.S.S.R.* 26, 483–5(1956)(Engl. translation).—See *C.A.* 50, 13883*b*. B. M. B.

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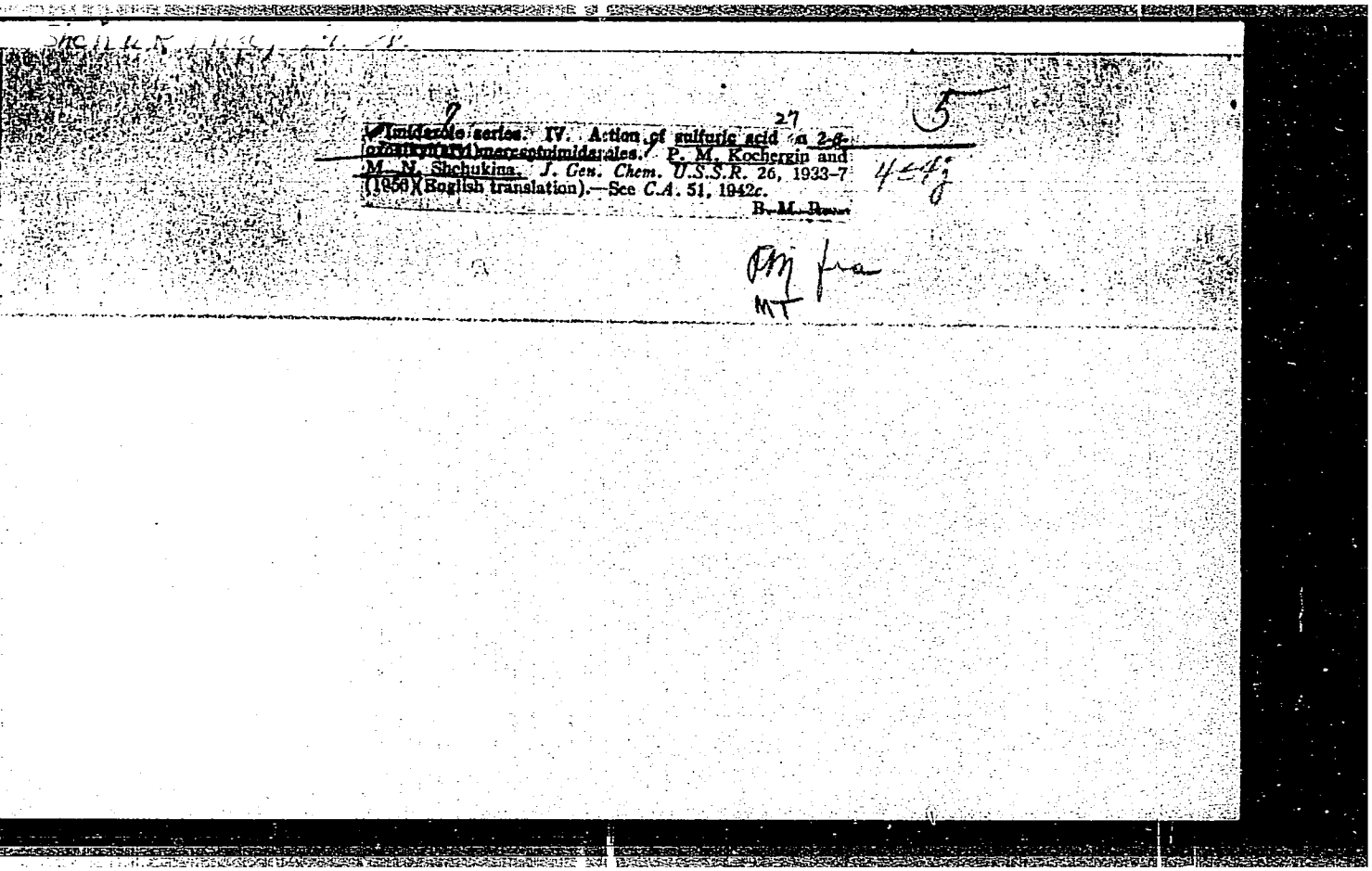
Imidazole series. Part 4: Reaction of sulfuric acid with 2-β-keto-alkyl(aryl)-mercaptoimidazoles. Zhur.ob.khim. 26 no.6:1723-1727 Je '56. (MIRA 11:1)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonikidze.
(Imidazole) (Sulfuric acid)



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Imidazole series. IV. Action of sulfuric acid on 2,6-
~~diphenyl-4(5)-mercaptoimidazoles.~~ P. M. Kochergin and
M. N. Shchukina. *J. Gen. Chem. U.S.S.R.* 26, 1933–7
(1956) (English translation).—See *C.A.* 51, 1942c.
B. M. Bzowej

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Sulfanilyl derivatives of natural α-amino acids and their analogs. Yuan Chen-e and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 26, 2872-82(1956).—The following derivs. of amino acids were found to be relatively weakly antibacterially active at best. To 11.25 g. $H_2NCH_2CO_2H$ in 20 ml. 40% NaOH and 50 ml. H_2O was added 37.5 g. *p*-

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$MeO_2CNHC_6H_4SO_2Cl$ with addn. of NaOH to maintain the alky. of the mixt. over 3 hrs.; after clarification with C and acidification there was obtained *p*-$MeO_2CNHC_6H_4SO_2NHCH_2CO_2H$, m. 169–70° (from 60% EtOH). Heating 8.15 g. DL-*p*-$MeO_2CNHC_6H_4SO_2NHCHMeCO_2H$ with 8 ml. concd. H_2SO_4 and 40 ml. EtOH 4 hrs. at 80–4° gave 91% *Et ester*, m. 144–4.5°. Heating 2.58 g. *p*-$H_2NC_6H_4SO_2NHCH_2CO_2Et$ with 1.25 ml. 80% $N_2H_4.H_2O$ in 26 ml. abs. EtOH 4 hrs. gave on evapn. 72% *p*-$H_2NC_6H_4SO_2NHCH_2CONHNH_2$, m. 160° (from 50% EtOH). Heating DL-*p*-$H_2NC_6H_4SO_2NHCHMeCO_2H$ with EtOH in the presence of HCl or H_2SO_4 gave 85.3% *Et ester*, m. 110–11°, which kept 3 days in EtOH-NH_3 gave 73.5% corresponding *amide*, m. 170.5–1.5° (from H_2O), which also formed on refluxing the corresponding *hydrazide* (I) with Raney Ni in 95% EtOH. To 1 g. I in 20 ml. EtOH was added at reflux 1 g. vanillin in 10 ml. EtOH, the mixt. kept 2 days at room temp. and heated 4 hrs. to reflux yielding yellow *p*-$H_2NC_6H_4SO_2NHCHMeCONHN{:}CHC_6H_3(OMe)OH$-3,4, m. 172–5°. Treatment of DL-serine in 50% NaOH with *p*-$AcNHC_6H_4SO_2Cl$ gave *N*-(*p*-*acetamidobenzenesulfonyl*)-DL-*serine* (II), m. 211–12° (from

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50% EtOH), which heated with 15% HCl, evapd. and neutralized with NaOAc gave 83.5% *N-p-acetamidobenzenesulfonyl-*DL*-serine*, m. 212–2.5° (from 50% EtOH), which with EtOH-HCl gave the *Et ester*, m. 86–7° (*HCl salt*, m. 175–81°). II (10 g.) and 1.9 g. KOH in 90 ml. H_2O were treated rapidly with 5.05 g. $AgNO_3$ in 50 ml. H_2O yielding 87.5% *Ag salt*, which after drying was suspended in C_6H_6 and treated 4.6 hrs. with MeI in the dark yielding, after refluxing 3 hrs., 70% II *Me ester*, m. 164–5°, which heated gradually with excess $SOCl_2$ to 65° gave 74% *p-AcNHC*$_6$*H*$_4$*SO*$_2$*NHCH*(*CH*$_3$*Cl*)*CO*$_2$*Me*, m. 130–6°, which treated with $EtOCS_2K$ overnight, acidified with HCl, the resulting xanthate deriv. (1.52 g.) taken up in EtOH, treated with 25% NH_4OH, allowed to stand 3 days, acidified with HCl, evapd., heated with 15% HCl until dissolved, then treated with 7.5 g. Zn 0.5 hr., evapd., and neutralized with NaOAc gave 53% *N-p-acetamidobenzenesulfonyl-*DL*-cysteine*, decomp. 182–92° (from H_2O with addn. of $Na_2S_2O_4$); the same formed from DL-cysteine and *p*-$AcNHC_6H_4SO_2Cl$ in 10% NaOH after the above treatment. Substitution of EtSNa for $EtOCS_2K$ in the above synthesis gave 38.2% *N-p-aminobenzenesulfonyl-S-ethyl-*DL*-cysteine HCl salt*, m. 159–62°, when the initially formed intermediate was refluxed with 15% HCl; the same formed from the above cysteine deriv. on treatment with EtI in aq. alc. NaOH. The use of BuSNa gave *N-p-aminobenzenesulfonyl-S-butyl-*DL*-cysteine HCl salt*, m. 143–52°. To 125 ml. NH_3 was added 2.5 g. L-cysteine followed by 0.96 g. Na and after decolorization of the blue soln. it was treated with 7.6 g. EtI and stirred 3 hrs. After evapn. of NH_3, stirring with H_2O 2 hrs., addn. of alkali to phenolphthalein endpoint, extn. of EtI with Et_2O and treatment of the aq. soln. by *p*-$AcNHC_6H_4SO_2Cl$ (III), it gave 38.9% *N-p-acetamidobenzenesulfonyl-S-ethyl-*L*-cysteine*, m. 180–2° (from 60% EtOH),

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$[\alpha]^{19}D$ 8°; this heated 1.5 hrs. with 15% HCl gave the *p-amino analog*, m. 152–3°, $[\alpha]^{19}D$ −12.8°. III and DL-glutamic acid in aq. NaOH gave, after hydrolysis of the Ac group with 15% HCl, 50.5% *N-p-aminobenzenesulfonyl-DL-glutamic acid*, m. 175–5.5°. To 13.05 g. 2-bromohexanoic acid in 45 ml. EtOH was added 21.1 g. p-$H_2NC_6H_4SO_2NHK$ and heated 8 hrs. on a steam bath yielding after sepn. of KBr, extn. with 10% Na_2CO_3, and acidification with AcOH 78% *N-p-aminobenzenesulfonyl-DL-norleucine*, m. 164°; *HCl salt*, m. 172–6°. Reaction of III with 6-aminohexanoic acid in aq. NaOH gave 72% *N-p-acetamidobenzenesulfonyl-e-leucine*, m. 146–7°; this gave the *p-amino analog*, m. 134°; Et ester, m. 94°. Similarly were prepd.: *p-AcNHC$_6$H$_4$SO$_2$NHCH(CO$_2$H)CH$_2$Ph*, m. 231°; its *p-amino analog* *Et ester*, m. 120–1°, and its *hydrazide*, m. 192–3°; *p-AcNHC$_6$H$_4$SO$_2$NHCH(CMe$_2$SH)CO$_2$H*, m. 224–9°, and its *p-amino analog*, m. 184–6°; *p-AcNHC$_6$H$_4$SO$_2$NHCH(CH$_2$CH$_2$SMe)CO$_2$H*, m. 149–51°, and its *p-amino analog*, m. 159–63°; *p-H$_2$NC$_6$H$_4$SO$_2$NHCH(CH$_2$CHMe$_2$)CO$_2$Et*, m. 105–6°, *its hydrazide*; *N-p-acetamidobenzenesulfonyltryptophane*, m. 238–9°, its *p-amino analog*, m. 188–90°. *N-p-Acetamidobenzenesulfonylproline* m., 228–9°, its *p-amino analog* m. 126–8°, and the *Et ester* of the latter m. 145–7°. Addn. of 17.2 g. iso-BuCHO to 11 g. 95% NaCN, 14 g. NH_4Cl, and 50 ml. H_2O with good stirring over 40 min., heating 1.5 hrs. at 60–3°, sepn. of the aminonitrile by extn. with Et_2O, and heating this with concd. HCl 10 hrs. gave on evapn. crude product which after crystn. from a little hot H_2O gave 8.8 g. DL-*leucine-HCl*, which with $NaHCO_3$ gave 36.5% DL-*leucine*, m. 268–70°.

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Synthesis of β-(*N*-2-chlorophenothiazyl)propionic acid, its derivatives and derivatives of β-*N*-phenothiazylpropionic acid. N. V. Savitskaya, Yu. S. Tsizin, and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 26, 2000–5(1956). —Heating 17.4 g. 3-chlorodiphenylamine, 3.8 g. S, and 0.2 g. iodine 1.3 hrs. at 160–80°, until H_2S evolution stopped gave 60.5% *2-chlorophenothiazine*, m. 199–200.5° (from MePh). This (10 g.) and 30 ml. CH_2:CHCN and 0.1 g. hydroquinone treated at room temp. with 2 ml. $PhNMe_3OH$ soln. (from 0.76 g. toluenesulfonate salt) and heated 1.5 hrs. at 80°, gave 81% β-(*N-2-chlorophenothiazyl*)*propionitrile* (I), m. 188–9° (from AcOH), which heated in sealed ampul with concd. H_2SO_4-EtOH 6 hrs. at 130–40°, then refluxed with 26% KOH 6 hrs. and acidified, gave 87% β-(*N-2-chlorophenothiazyl*)*propionic acid* (II), m. 156.5–58° (from MeOH); if the treatment with KOH is omitted there is formed the *Et ester* (III), $b_{0.4}$ 205–9°, m. 64.5–66° (from petr. ether). Hydrogenation of I over Raney Ni in EtOH under 10 atm. NH_3 at 100–10° and 90 atm. H_2 gave *N-(3-aminopropyl)-2-chlorophenothiazine; HCl salt*, m. 233–5° (from dry EtOH). III and satd. NH_3 in dry EtOH gave in 24 hrs. β-(*N-2-chlorophenothiazyl*)*propionamide*, m.

143.5–5.5° (from C_6H_6); similarly III and 65% $N_2H_4.H_2O$ in EtOH heated 28 hrs. on steam bath gave the corresponding *hydrazide*, m. 132.5–3.5° (from MeOH); *p-acetamidobenzylidene deriv.*, m. 236–7°. II and PCl_5 in C_6H_6 gave the crude acyl chloride which was freed of solvent and $POCl_3$ by mild heating *in vacuo* and washing with C_6H_6, and this solid chloride was refluxed with $HOCH_2CH_2Cl$ 1 hrs. yielding 70% II *2-chloroethyl ester*, m. 83–4° (from EtOAc), which heated with Me_2NNH_2 5.5 hrs. at 100° in ampul gave 46% *1,1-dimethyl-1-[2'-(β-N-2-chlorophenothiazyl)propionyloxyethyl]hydrazonium chloride*, m. 184–5° (from EtOAc-EtOH). Heating *β-N-phenothiazylpropionic acid* with MeOH in the presence of H_2SO_4 6 hrs. gave its *Me ester*, 83%, m. 64.5–5.5°, b_1 210–14°; *Et ester*, prepd. similarly to above from the corresponding *nitrile* in 34% yield, m. 63.5°, $b_{0.4}$ 195–202°. The free acid treated with PCl_5 as above, followed by NH_3, gave *β-N-phenothiazylpropionamide*, m. 125–6° (25%) (from aq. EtOH). The Et ester and $N_2H_4.H_2O$ heated 28 hrs. gave the *hydrazide*, decomp. 98–9°, whose *p-acetamidobenzylidene deriv.*, m. 192–3°, and *4-hydroxy-3-methoxybenzylidene deriv.*, m. 200.5–202° (from AcOH). Treatment of the acyl chloride, prepd. as above, with $Me_2NCH_2CH_2OH$ in C_6H_6 gave *β-N-phenothiazylpropionic acid dimethylaminoethyl ester*, 66%, b. 214–16°; *HCl salt*, m. 141.5–2.5° (from PhCl). Similarly the acyl chloride and $ClCH_2CH_2OH$ gave the *2-chloroethyl ester*, m. 75–6°, which with Me_2NNH_2 kept 2 days at room temp. and 3 days at 0° gave *1,1-dimethyl-1-[2'-(β-N-phenothiazyl)propionyloxyethyl]hydrazonium chloride*, m. 174.5–5.5° (from abs. EtOH).

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Imidazole series. VI. Action of bromoacetaldehyde and its derivatives on some 2-mercaptoimidazoles. P. M. Kocheregin and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 26, 2015–16(1956); cf. *C.A.* 51, 5050b.—On the basis of structures of intermediates described below, the mechanism for closure of imidazo[2,1-*b*]thiazole rings appears to proceed by formation of 2-oxoalkylimidazolyl sulfides, which cyclize at the carbonyl group and the NH group of the imidazole portion, yielding 3-hydroxyimidazo-[2,1-*b*]thiazolines, which then lose H_2O yielding the final product. The structures of the products described below are confirmed by infrared spectra which are reproduced. To 1.3 g. Na dissolved in 50 ml. abs. EtOH was added 10 g. 4(5)-phenyl-2-mercaptoimidazole (I), followed by 11.3 g. $BrCH_2CH(OEt)_2$, and the mixt. refluxed 11 hrs., filtered from NaBr, washed with H_2O, and evapd. yielding 98.2% *4(5)-phenylimidazol-2-ylmercaptoacetaldehyde di-Et acetal*, a viscous oil, whose *picrate*, m. 126–7°; the analogous *di-Me acetal*, an oil, was prepd. similarly. The di-Et acetal (II) (8.9 g.) was refluxed 1.5 hrs. with 20 ml. $POCl_3$, freed of excess $POCl_3$ *in vacuo*, treated with H_2O and neutralized with $NaHCO_3$, and extd. with $CHCl_3$, yielding 75.1% *3-ethoxy-6-phenylimidazo[2,1-b]thiazoline*, m. 122° (from EtOH) (*picrate*, decomp. 197–8°); similarly the di-Me acetal gave the *3-methoxy analog*, an oil, whose *HCl salt*, decomp. 141–2°, and

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on treatment with $NaHCO_3$ gave the pure *free base*, m. 71.5–2.5°; *picrate*, decomp. 172–3°. Refluxing 8.7 g. EtOCHBr-CH_2Br in 70 ml. H_2O until a soln. formed, followed by addn. of 6.6 g. I and refluxing 1 hr., neutralization with $NaHCO_3$ and filtration gave 8 g. *3-hydroxy-6-phenylimidazo[2,1-b]thiazoline*, decomp. 160–1° (*HCl salt*, decomp. 163–5°; *picrate*, decomp. 145–6°, forms a *dihydrate*. The same components react similarly in refluxing C_6H_6; the same product also formed in 86% yield on refluxing II with 38% HCl 1.3 hrs. or on standing 1 day in alc. HCl. Refluxing 6 g. 4(5)-*p*-nitrophenyl-2-mercaptoimidazole with 6.3 g. EtOCHBr-CH_2Br in H_2O 3 hrs. gave after neutralization 96.5% *3-hydroxy-6-p-nitrophenylimidazo[2,1-b]thiazoline* (IIa), decomp. 203–4° (from Me_2CO). Refluxing 2 g. 2-aminothiazole with 3.97 g. $BzCH_2Br$ in 45 ml. EtOH 1.5 hrs., evapg. and treating with Et_2O gave 90.9% *6-phenylimidazo[2,1-b]thiazole HBr salt*, m. 114–16°, which with $NaHCO_3$ gave the *free base* (III), m. 146–6.5° (from aq. EtOH); *HCl salt*, m. 153–4°; *sulfate*, m. 210–11° (*monohydrate*, from EtOH); *picrate*, m. 223–3.5°. II (1.4 g.) in 6.5 ml. 95% H_2SO_4 heated to 50° over 0.5 hr., then poured into 12–15 ml. H_2O and heated on a steam bath 1 hr., neutralized with $NaHCO_3$, and extd. with $CHCl_3$ yielded the above product, isolated as *picrate*, m. 223°, in 0.15-g. yield. III formed in 74.1% yield on heating 1 g. 3-hydroxy-6-phenylimidazo[2, 1-*b*]thiazoline with 6 ml. 95% H_2SO_4 7–10 min. at 30° and keeping several hrs. at room temp.; the yield was 67.8% if $POCl_3$ was substituted for H_2SO_4 and the mixt. refluxed 10 min. Similarly, up to 98% yields were obtained on heating the 3-MeO or 3-EtO derivs. of phenylimidazothiazoline with 95% H_2SO_4 as above. IIa (3 g.) refluxed 2 hrs. with 50 ml. $POCl_3$ gave after aq. treatment and addn.

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of Na_2CO_3, 96.4% *6-p-nitrophenylimidazo[2,1-b]thiazole*, m. 238–4° (from AcOH). Heating 3.5 g. 95.6% H_2SO_4 with 0.3 g. 3-methoxy-6-phenylimidazo[2,1-*b*]thiazoline HCl salt 0.5 hr. on a steam bath, cooling, and dilg. with 20 ml. ice H_2O, gave 79.7% *6-p-sulfophenylimidazo[2,1-b]thiazole* (IV), spindly crystals (from H_2O), does not m. 360°; *monohydrate* loses H_2O at 100°; the 3-EtO analog gave the same product in 77% yield, as did the 3-HO analog in 84.8% yield (in this case a small amount of relatively insoluble III also formed). Heating III with 95% H_2SO_4 0.5 hr. at 100° gave 64.4% IV. VII. Action of acetic anhydride on 2-β-oxoalkyl(aryl)mercaptoimidazoles. P. M. Kochergin. *Ibid.* 2016–24.—Refluxing 1.25 g. 4(5)-phenyl-2-acetonylmercaptoimidazole with 6 ml. Ac_2O 5–7 min., cooling, and filtering gave 1.21 g. *1-acetyl-5-phenyl-2-acetonylmercaptoimidazole*, m. 158–9°, with total yield of 98% being obtained after concn. of the mother liquors. Similarly, from corresponding imidazoles were prepd. the following *1-acetyl-5-phenyl(or p-nitrophenyl)-2-β-oxoalkyl(aryl)mercaptoimidazoles*: *5-phenyl-2-(1-methyl-2-oxopropyl)*, 99.7%, m. 152–4°; *5-phenyl-2-(m-nitroacetophenonyl)*, m. 161–2°; *5-phenyl-2-(2-cyclohexanonyl)*, 78.1%, m. 156–7°; *5-p-nitrophenyl-2-acetonyl*, 95.7%, m. 182–3°. Heating 0.7 g. 4(5)-phenyl-2-p-nitrophenacylmercaptoimidazole with 15 ml. Ac_2O 8–10 min. at 100°, removing Ac_2O *in vacuo*, and cooling gave 76% *1-acetyl-5-phenyl-2-p-nitrophenylmercaptoimidazole*, m. 169–70° (from EtOH); if the reaction mixt. is refluxed, the same product forms along with *2-p-nitrobenzoyl-5-methyl-5-phenylimidazo-*

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[2,1-b]thiazole, m. 190°, isolated by treating the mother liquors with alc. HCl. Refluxing 0.8 g. 1-acetyl-5-phenyl-2-acetonylmercaptoimidazole with 0.8 g. NaOAc and 4.5 ml. Ac_2O 0.5 hr. gave 98.6% *2-acetyl-5-phenylimidazo[2,1-b]-thiazole*, m. 150–1° (from EtOH). Similarly was prepd. *3-methylimidazo[2,1-b]thiazolyl-2-benzoyl analog*, m. 227–8°, and *2-acetyl-3-methylimidazo[2,1-b]thiazolyl-5-p-nitrophenyl analog*, m. 186–7°, as well as *2-m-nitrobenzoyl-3-methyl-5-phenylimidazo[2,1-b]thiazole*, m. 144–5°, and its *2-p-nitrobenzoyl analog*, m. 190°. Refluxing 5 g. 4(5)-phenyl-2-mercaptoimidazole in 75 ml. EtOH with 3.85 g. 3-chloro-2,4-pentanedione 15 min., followed by evapn. in vacuo, gave 99.2% *4(5)-phenyl-2-(α-acetoacetonyl)-mercaptoimidazole*, m. 135–6° (*HCl salt* (I), decomp. 148–51°). To 0.56 g. Na in 75 ml. EtOH was added 5.4 g. 4(5)-*p*-nitrophenyl-2-mercaptoimidazole and 3.4 g. 3-chloro-2,4-pentanedione and the mixt. refluxed 1 hr. gave 91% *4(5)-p-nitrophenyl-2-(α-acetylacetonyl)mercaptoimidazole* (II), m. 144–5° (from EtOAc). I (2 g.) refluxed 1 hr. in 10 ml. BuOH gave on cooling 74.5% *2-acetyl-5-methyl-6-phenylimidazo[2,1-b]thiazole*, m. 203–3.5°, isolated as *HCl salt*, m. 232–4°. Refluxing 2.7 g. II in 40 ml. $POCl_3$ 0.5 hr.,

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followed by removal of $POCl_3$ *in vacuo* and treatment with aq. $NaHCO_3$ gave 98% *2-acetyl-3-methyl-6-p-nitrophenylimidazo[2,1-b]thiazole*, m. 281–1.5° (from AcOH); this formed in 67% yield from 4-methyl-5-acetyl-2-aminothiazole and $BrCH_2COC_6H_4NO_2$-*p* after refluxing 2 hrs. in EtOH, and 1 hr. with AcOH after removal of EtOH. G. M. K.

Cyclization of thiobiurets[2] to substituted 1,2,4-thiadiazoles.[7] F. Kurzer (Roy. Free Hosp. School Med., London). *Chem. & Ind.* (London) 1956, 1482.—Dealkylation of PhNHCSNHC(OR):NH (I) gave $PhNHCSNHCONH_2$ (II), m. 159–60°; dehydrogenation of I or II with Br or H_2O_2 gave good yields of S.N:C(OR).N:CNHPh (III). R and m.p. were given for I: Me, 129–30°; Et, 98–9°. For III: Me, 158–9°; Et, 167–8°; H, 212–13°. G. R. Yohe

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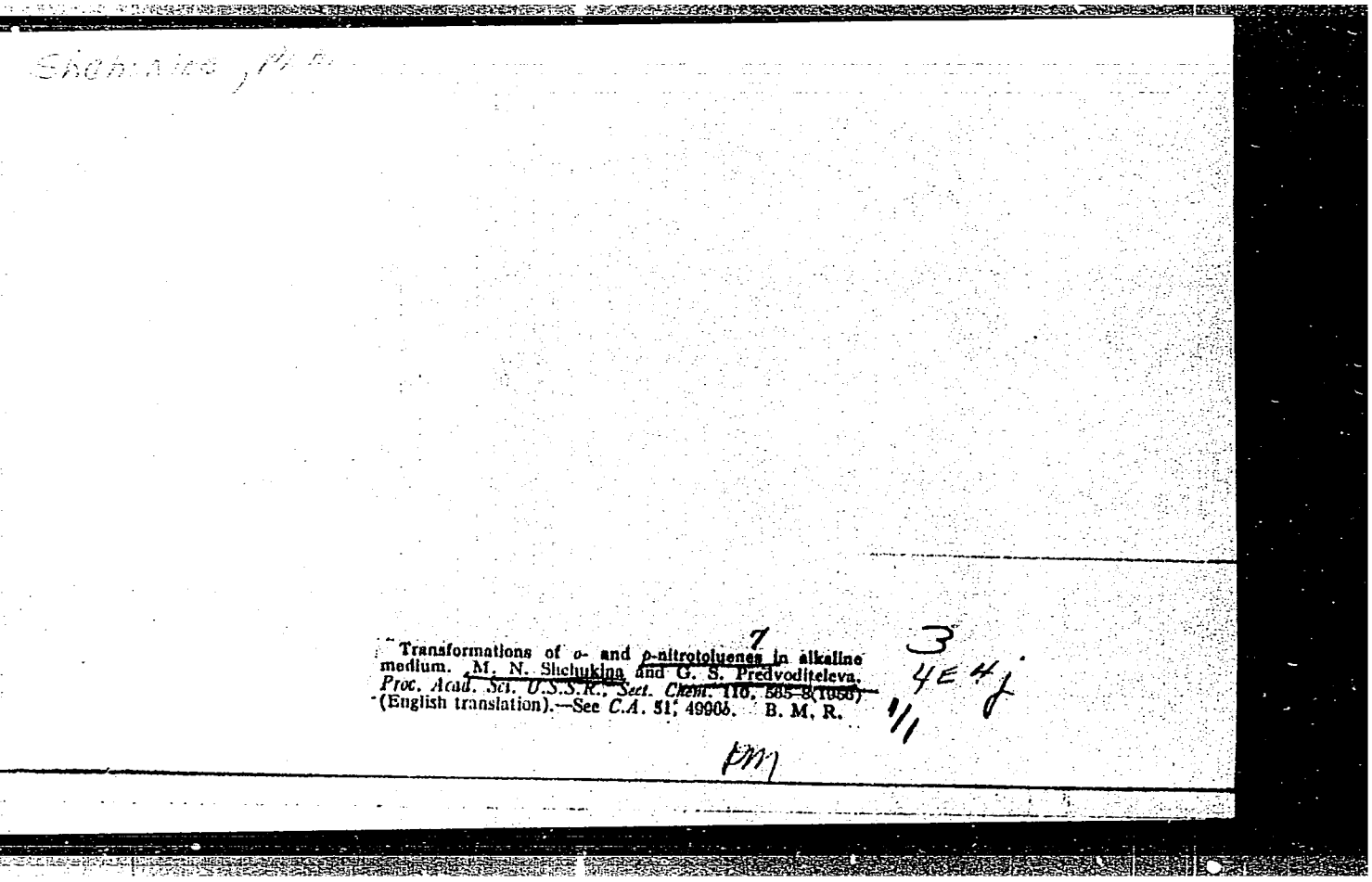
SHCHUKINA, M. N.

Transformations of *o*- and *p*-nitrotoluenes in alkaline medium. M. N. Shchukina and G. S. Predvoditeleva (S. Ordzhonikidze All-Union Chem. Pharm. Sci. Res. Inst., Moscow). *Doklady Akad. Nauk S.S.S.R.* 110, 230-3(1956); cf. Ger. 86,874; Plisov, *C.A.* 24, 1108.—While basic treatment of *o*-$MeC_6H_4NO_2$ (I) results in reactions probably proceeding through intermediates of an anthranil type, the *p*-isomer must form similar polymeric intermediates. I in NaOH with S should yield *o*-$H_2NC_6H_4CHO$. The reaction yields 14% of this aldehyde and some *o*-$MeC_6H_4NH_2$. If the soln. of S in NaOH is added to the mixt. only after I had been refluxed with 20% aq. alc. NaOH for several hrs., there is obtained 15% 2-indazylbenzyl alc. Anthranil with S and NaOH gave anthranilic acid and *o*-$H_2NC_6H_4CHO$; phenyl-*N*-phenylnitrone gave $PhCH{:}NPh$, while *p*-nitrophenyl-*N*-*p*-tolylnitrone gave *p*-$MeC_6H_4NH_2$ and an anhydropolymer of *p*-$H_2NC_6H_4CHO$. The red substance formed from *p*-$MeC_6H_4NO_2$ and NaOH is chemically inert to acids, bases, and oxidation-reduction reagents; its spectrum (infrared) does not have the bands typical of N—O group of nitrones (butyl-*N*-methylnitrone and *N*-oxides of pyridine and Me_3N show intense bands at 1185–1250 cm.$^{-1}$ and 920–950 cm.$^{-1}$); hence the groups which connect the polymer links are not nitrone groups but probably amide links. This is confirmed by the fact that *p*-nitrophenyl-*N*-*p*-tolylnitrone treated with aq. alc. NaOH gave a very inert polymer, which with piperidine gave *p*-nitrobenzo-*p*-toluidide, which indicates that the initially formed nitrone undergoes under the action of alkali, a rearrangement of the Beckmann type, forming a *p*-linked polyamide. I with NaOH may be represented by formation of unstable lactam from the initially formed anthranil; the latter gives rise to a variety of products depending on the subsequent treatment. G. M. Kosolapoff.



Shchukina, M. N.

Transformations of o- and p-nitrotoluenes in alkaline medium. M. N. Shchukina and G. S. Predvoditeleva. *Proc. Acad. Sci. U.S.S.R., Sect. Chem.* 110, 585-8(1956) (English translation).—See *C.A.* 51, 4990b. B. M. R.

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SHCHUKINA, M. N.

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1- 4E4f

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3-Dimethylaminopropanol. M. N. Shchukina, N. V. Savitskaya, T. V. Gortinskaya, Yu. S. Tsizin, and V. G. Samolovova. U.S.S.R. 105,447, May 25, 1957. The compd. is obtained by reduction of ethylene cyanohydrin and methylation of the resulting 3-aminopropanol. The reduction of ethylene cyanohydrin is carried out in a ammoniacal-alc. soln. and the methylation is done with CH_2O in HCO_2H.
M. Hoseh

SHCHUKINA, M.N.

Distr: 4E4j

2,5-Di(4-pyridyl)-1-amino-1,3,4-triazole and its derivatives. V. G. Yashunskii, L. N. Pavlov, V. G. Ermolaiva, and M. N. Shchukina. *Khim. Nauka i Prom.* 2, 653(1957).—If the condensation of isonicotinic acid with hydrazine hydrate besides the by-product 1,2-diisonicotinoyl a new product was found which is probably 2,5-di(4-pyridyl)-1-amino-1,3,4-triazole (I), stable in boiling HCl. K_2MnO_4 and concd. HNO_3 reacted with I to give *2,5-di(4-pyridyl)-1,3,4-triazole* (II), m. 286–9°. Its di-HCl salt (m. 300–2°) and its dipicrate (m. 257–9°) were prepd. Boiling I with PhCHO at 150–5° gave the benzaldiazine derivs. of II (m. 197–200°) and of 2,4-di(4-pyridyl)triazole, m. 286–9°. I. Beneowitz.

SHCHUKINA, M. N.

"Complexon-IV" and its analogs. V. G. Vashunskii and M. N. Shchukina. *Khim. Nauka i Prom.* 2, 662-3 (1957).—*cis*- (I) and *trans*- (II) -1,2-Diaminocyclohexane were prepd. The expected reaction of I with $ClCH_2CO_2H$ (cf. Schwartzenbach, *et al.*, *C.A.* 44, 548c) did not take place. On the other hand II reacted, giving, *1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid* (III), the properties of which were identical with those of "complexon-IV" which S. believed was the cis isomer. The *trans-1,2-diaminocyclopentane-N,N,N',N'-tetraacetic acid* (IV) and the corresponding *butane* analog (V) were prepd. by condensation of the respective diamine with $ClCH_2CO_2H$. The values of pK_1, pK_2, pK_3, and the stability consts. of the complex CaX^- of IV were 2.4, 3.3, 7.56, 10.80, and 12.2; and of V 2.7, 2.8, 5.80, 9.75, and 8.0. The corresponding values of ethylenediamine-*N,N,N',N'*-tetraacetic acid (given for comparison) were 1.996, 2.672, 6.161, 10.26, and 10.59. V was the least stable. It was concluded that the essential factor for increased stability of the internal complex of metalocycles was that the amino groups be close to each other and that their free rotation about the C-1–C-2 bond be hindered.

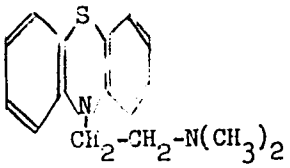
I. Bencowitz

122. Synthesis of Aminazine and Other Phenothiazine Derivatives

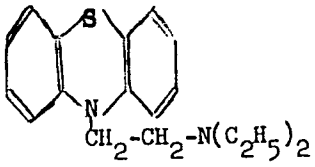
"On the Synthesis of Aminazine and Its Analogues," by N. M. Shchukina, N. V. Savitskaya, and Yu. S. Tsizin, All-Union Scientific-Research Chemicopharmaceutical Institute imeni S. Ordzhonikidze, Meditsinskaya Promyshlennost' SSSR, Vol 11, No 3, Mar 57, pp 20-24

This article describes a method of synthesizing aminazine and its analogues--etizine, dinezine, diprozine, and mul'tezine -- all phenothiazine derivatives. All have been found to possess important pharmacological properties, i.e., they act as spasmolytics and sedatives, affect the

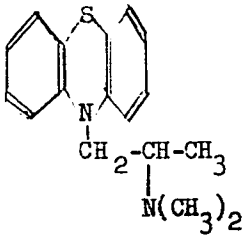
central nervous system, and are used as therapeutic agents in nervous diseases and in the practice of psychiatry. Aminazine is the only one of the group of phenothiazine derivatives in which there is substitution in the nucleus. In all other cases, only the nitrogen is replaced by N-alkylaminoalkyl radicals. They are easily synthesized by the heating of phenothiazine with haloidoalkyl-aminoalkyl compounds and alkaline reagents. The best results are obtained when condensation is carried out with sodium hydroxide, with the water and immiscible solvents -- benzene and toluol -- being continuously drained off, a method developed at the experimental plant of the All-Union Scientific-Research Chemicopharmaceutical Institute by L. I. Morozovskaya and M. A. Vorob'yev. N-dialkylaminoalkylphenothiazines are obtained having the following structural formulas:

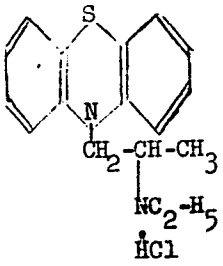


Etizine (anergan)

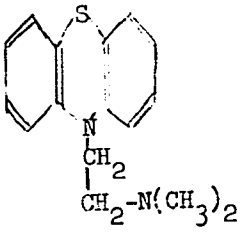


Dinezine (diparkol)



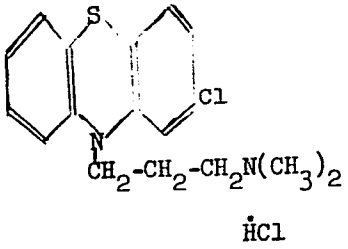


Diprozine (fenergan)



Promazine

Parfezine (parsidol)



Aminazine (largactile, Chlorpromazine)

Other ways of compounding the dialkylaminoalkyl radical with phenothiazine by a method of condensing phenothiazine with substances having an active unsaturated system or with substances with an oxide radical are described. (U)

GORTINSKAYA, T.V.; SAVITSKAYA, N.V.; SAMOLOVOVA, V.G.; TSIZIN, Yu.S.; SHCHUKINA, M.N.

Obtaining dimethylaminopropanol from ethylene cyanohydrin. Med. prom. 11 no.4:23-25 Ap '57. (MLRA 10:6)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(PROPANOL) (HYDRACRYLONITRILE)

SHCHUKINA, M.N.; GOLOMBIK, E.S. [deceased]

Producing phenylacetamide. Med.prom. 11 no.7:42-44 Jl '57. (MLRA 10:8)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze
(ACETANILIDE)

YASHUNSKIY, V.G.; PAVLOV, L.N.; YERMOLAYEVA, V.G.; SHCHUKINA, M.N.

By-product of the condensation of isonicotinic acid and hydrazine hydrate. Med.prom. 11 no.12:38-40 D '57. (MIRA 11:2)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(ISONICOTINIC ACID) (HYDRAZINE) (TRIAZOLE)

SHUKINA, M.N. (Moskva); YUAN' CHEN-YE [Yuan Cheng-i] (Shankhay).

Mercapto acids and mercaptocarboxylic acids. Usp. khim. 26 no.5: 608-624 My '57. (MLRA 10:6)
(Mercapto compounds)

SHCHUKINA, M. N.

Mercapto analogs of lysine and some of their derivatives. I. Synthesis of ε-mercapto-α-aminocaproic acid and its *S*-alkyl and *N*-sulfanilyl derivatives. Chen-E Yuan and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 27, 824–31(1957).—Heating 74 g. $EtO_2C(CH_2)_3CH$, 66 g. $CS(NH_2)_2$, and 315 ml. 48% HBr 10 hrs. on a steam bath, followed by addn. of 644 ml. 20% NaOH with cooling and refluxing under N 3 hrs., heating 1 hr. at 120° in an N stream, cooling, acidifying and extg. with Et_2O gave 3.1 g. $HO_2C(CH_2)_5SH$ (I), $b_{0.4}$ 112–16°, and its *disulfide*, 0.9 g., $b_{0.4}$ 163–70°, m. 80–2°. Heating 16.5 g. KSH in 200 ml. EtOH with 33.45 g. $EtO_2C(CH_2)_4Br$ 2 hrs. gave 64.5% $EtO_2C(CH_2)_5SH$, $b_{0.7}$ 84–5°, n_D^{20} 1.4503, d_{20} 0.9895; *P-o-nitrobenzoyl* deriv., yellow solid. The ester formed from the acid and EtOH-HCl in 66% yield. The ester (14.08 g.) heated with 1.84 g. Na in 60 ml. EtOH and 13.75 g. EtI 1 hr. at 60–70°, then refluxed 3 hrs. gave after filtration, concn., treatment with Na_2CO_3 and extn. with Et_2O, 14.9 g. crude or 11.8 g. pure $EtS(CH_2)_5CO_2Et$ (II), $b_{0.5}$ 130–4°, $b_{1.4}$ 150°, n_D^{20} 1.4620, d_{20} 0.9675; similarly was prepd. 75% *S-benzyl analog* (III), $b_{0.6}$ 172–3°, 1.5223, 1.0452, which loses the $PhCH_2$ group in liquid NH_3 under action of Na yielding I. II (3.5 g.) with 2.3 g. 27.3% H_2O_2 in 25 ml. AcOH in 3 days gave 56.5% $EtS(O)(CH_2)_5CO_2Et$, $b_{0.4}$ 190–200°; similarly was prepd. the *S-benzyl analog*, m. 56–7°. II (3.1 g.) in 0.345 g. Na and 15 ml. dry EtOH was treated with 55 ml. H_2O and refluxed 13 hrs. yielding on evapn. 70.8% $EtS(CH_2)_5CO_2Na$, does not m. 300°; the Na salt of the *S-benzyl analog*, was prepd. similarly. III (13.3 g.) and an unstated amt. of $(CO_2Et)_2$ added to EtONa from 3) ml. EtOH and 1.15 g. Na, heated at 50–60°/100 mm. 2 hrs., dild. with H_2O, acidified with H_2SO_4, and extd. with Et_2O, gave 65% $PhCH_2S(CH_2)_4CH(CO_2Et)_2$ (IV), $b_{0.4}$ 190–6°;

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this kept with EtOH satd. with NH_3 1 day gave the *mono-amide*, m. 96–8° (from EtOH). IV (13.35 g.) in 0.91 g. Na and 18 ml. dry EtOH treated at 2° with 4.5 g. BuONO and stirred 2.5 hrs. at room temp. gave after evapn., dilu. with H_2O, and extn. with Et_2O 80% oily *oximino deriv.*, which (6.02 g.) in 15 ml. AcOH and 15 ml. Ac_2O treated slowly with 5 g. Zn dust activated with HCl and stirred 2 hrs., filtered and concd., gave 72% $PhCH_2S(CH_2)_4CH(CO_2Et)NHAc$, m. 125–7° (from EtOH-$Et_2O$), which heated at 100° 18 hrs. with 15% HCl, washed with Et_2O, evapd. several times to remove excess HCl, clarified with C and treated in aq. soln. with 3 ml. pyridine gave 78% *$PhCH_2S(CH_2)_4CH(NH_2)CO_2H$* (V), decomp. 238–42° (from EtOH-Et_2O). This (1.45 g.) in 80 ml. liquid NH_3 treated with 0.204 g. Na and stirred 3 hrs. at room temp., then dild. with H_2O, acidified with HCl, extd. with Et_2O, and the org. layer evapd. and extd. with ale. HCl gave on evapn. of the ext. 0.75 g. *$HS(CH_2)_4CH(NH_2)CO_2H$ HCl salt*, m. 228–34°. This with *p*-$AcNHC_6H_4SO_2Cl$ and $Na_2S_2O_4$ gave the oily acetylsulfanilyl deriv., which heated 1 hr. with 15% HCl at 100° gave 64% *$HS(CH_2)_4CH(NHC_6H_4SO_2H\text{-}NH_2\text{-}p)CO_2H$ HCl salt* (VI), decomp. 203–8° (from 20% HCl). V treated as above with Na in liquid NH_3 gave on treatment with BuI 70.5% *$BuS(CH_2)_4CH(NH_2)CO_2H$*, decomp. [illegible]–2° (from H_2O). This with *p*-$AcNHC_6H_4SO_2Cl$ in [illegible] NaOH followed by heating with 15% HCl 1 hr. gave a product, m. 35–43°; after treatment with 10% HCl it [illegible] *$S(CH_2)_4CH(NHO_2SC_6H_4NH_2\text{-}p)CO_2H$ HCl salt*, m. 235–43° (from 10% HCl); the same product formed by shaking VI with BuI under N in aq. ale. NaOH.

G. M. Kosolapoff

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Shchukina, M. N.

Mercapto analogs of lysine and some of their derivatives. II. Synthesis of α-mercapto-ω-amino- and α,ω-dimercaptocarboic acids and their *S*-alkyl and *N*-sulfanilyl derivatives. Chen-E Yuan and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Sci.-Research Inst., Moscow). *Zhur. Obshchei Khim.* 27, 1103–8(1957); cf. *C.A.* 51, 16291*e*. —Heating 1.5 g. KSH and 3.14 g. $BzNHCH_2(CH_2)_3CHBrCO_2H$ in EtOH 1 hr. gave a ppt. which after extn. with EtOH and concn. of the ext. gave an oil which after repptn. from Na_2CO_3 with HCl gave $BzNH(CH_2)_3CH(SH)CO_2H$, m. 152–7° (50% EtOH); hydrolysis with 20% HCl 18 hrs. and treatment of the crude product with $Pb(OAc)_2$ gave a cryst. Pb mercaptide which decompd. with H_2S yielded 41.5% $H_2N(CH_2)_4CH(SH)CO_2H.HCl$ (I) after evapn. from aq. HCl; the pure salt, decomp. 122–4.5° (EtOH-Et_2O). This treated with dry HCl in abs. EtOH 2 days gave the *Et ester*, $b_{2.1}$ 182–4°, which is sol. in aq. NaOH, but the solns. slowly ppt. the disulfide oxidation product. I in EtOH-2*N* NaOH treated with BuI in N at room temp. 15 hrs. gave 82.3% $H_2N(CH_2)_4CH(SBu)CO_2H$, isolated as *HCl salt* (II), m. 228–30°. Heating *p*-$AcNHC_6H_4SO_2NH(CH_2)_4CH_2CO_2H$ in $CHCl_3$ with $SOCl_2$ 0.5 hr., followed by treatment with Br in $CHCl_3$ at 50°, and finally at 90° 1.5 hrs. gave, after ice treatment, an unstated yield of *p*-$AcNHC_6H_4SO_2NH(CH_2)_4CHBrCO_2H$, decomp. 125–8° (aq. EtOH). This with alc. KSH, as above, gave the expected mercapto deriv., which in crude state was refluxed 1 hr. with 15% HCl, yielding 50.5% *p*-$H_2NC_6H_4SO_2NH(CH_2)_4CH(SH)CO_2H.HCl$ (III), decomp. 182–7°; this also formed in 37.8% yield on treatment of 1.2 g. I with 0.2 g. Na hydrosulfite and 1.4 g. *p*-$AcNHC_6H_4SO_2Cl$. The latter reacted with

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II in *N* NaOH to yield after hydrolysis with HCl 78.5% *p*-$H_2NC_6H_4SO_2NH(CH_2)_4CH(SBu)CO_2H.HCl$, m. 171.5–2.5° (10% HCl), which also formed from III and BuI in *N* NaOH in EtOH, the yield being 46.2%. Refluxing 15.3 g. KSH with 16 g. $Br(CH_2)_4CHBrCO_2Et$ in EtOH 18 hrs. gave 25% $HS(CH_2)_4CH(SH)CO_2Et$, (IV) $b_{1.1}$ 100–2°, d_{20} 0.9865, n_D^{20} 1.4452, and 41.7% $S.S.(CH_2)_4.CHCO_2Et$, $b_{0.9}$ 187.5–9°. Refluxing IV with EtI in EtOH 12 hrs. gave $EtS(CH_2)_4CH(SEt)CO_2Et$, 81.1%, $b_{0.5}$ 134–6°, d_{20} 0.9989, n_D^{20} 1.4753.

G. M. Kosolapoff

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Shchukina, M. N.

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V Synthesis of mercapto amino compounds. I. Synthesis of 11-amino-10-hydroxyundecanoic acid and related compounds. Yu. V. Markova, K. K. Kuz'mina, and M. N. Shchukina (S. Ordzhonikidze All Union Chem. Pharm. Sci.-Research Inst., Moscow). *Zhur. Obshchei Khim.* 27, 1270–3(1957).—Oxidation of 24.8 g. Me 10-undecenoate in $CHCl_3$ with BzO_3H overnight at 0° gave 67.9% *Me 10,11-epoxyundecanoate* (I), b_{11} 168–74°. Similarly, *1-benzoyl-1-decene* gave 76.7% corresponding *oxide*, m. 37°, b_{11} 225–31°. This with Et_2O-HCl in 2 hrs. gave *1-chloro-2-hydroxy-10-benzoyldecane*, m. 62–4°. Similarly, I gave 100% *Me 11-chloro-10-hydroxyundecanoate*, b_{20} 200–2°, m. 38–41°, whose *free acid* in 1 day in 25% NH_4OH gave 90% *11-amino-10-hydroxyundecanoic acid*, m. 199–200°; *HCl salt*, m. 127–8°; *HBr salt*, m. 119–21°. Heating 1-benzoyl-1-decene oxide with 33% NH_4OH in an ampul 8 hrs. at 150° gave a little *bis(10-benzoyl-2-hydroxydecyl)amine*, m. 116–18°. Heating 1-chloro-2-hydroxy-10-benzoyldecane with 33% NH_4OH as above gave a low yield of the above secondary amine; but similar reaction with 18% alc. $MeNH_2$ gave a little *1-methylamino-2-hydroxy-10-benzoyldecane*, m. 78–80.5°. II. Synthesis of 11-amino-10-mercaptoundecanoic acid and related compounds. *Ibid.* 1274–6.—Heating 11-amino-10-hydroxyundecanoic acid HCl salt (10 g.) and 30 ml. $SOCl_2$, finally at 50–60°, gave 86% *11-amino-10-chloroundecanoyl chloride HCl salt*, decomp. 117.5–19.5°, which refluxed in abs. EtOH 8 hrs. gave 63% Et *11-amino-10-chloroundecanoate HCl salt*, m. 133–5° (EtOH). This (2 g.) in 15 ml. H_2O

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Markova, K. V., Kuz'mina, K. K. and ...

was treated with 0.5 g. CS_2 and 2.5 ml. 22% NaOH, yielding 75% *2-mercapto-5-(8-carbethoxyoctyl)thiazoline* (I), m. 55.5–7.5° (aq. EtOH). Similarly was prepd. the *8-carboxyoctyl analog*, m. 139–41°, which required merely the use of a larger amt. of 22% NaOH. I (3 g.) and 50 ml. concd. HCl in a sealed tube 5 hrs. at 150° gave 50% *11-amino-10-mercaptoundecanoic acid HCl salt*, m. 139–42° (EtOH). Shaking 2.14 g. Me 10-undecenoate oxide with 1.54 g. $HSCH_2CH_2NH_2$ in H_2O 50 hrs. gave 10% $MeO_2C(CH_2)_8CH(OH)CH_2SCH_2CH_2NHCH_2CH(OH)(CH_2)_8CO_2Me$, m. 68–73°. Similar reaction using 10-benzoyl-1-decene oxide gave a low yield of $Bz(CH_2)_8CH(OH)CH_2SCH_2CH_2NHCH_2CH(OH)(CH_2)_8Bz$, m. 92–4° (EtOH). G. M. Kosolapoff

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MARKOVA, Yu.V.; KUZ'MINA, K.K.; SHCHUKINA, M.N.

Synthesis of mercapto amino compounds. Part 2: Synthesis of 11-amino-10-mercapto hendecanoic acid and related compounds. Zhur.ob.khim. 27 no.5:1274-1276 My '57. (MLRA 10:8)

1.Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(Hendecanoic acid) (Mercapto compounds)

Shchukina, M. N.

Distr: 4E4j/4E2c(j)/4E3d

Synthesis of 2,5- and 2,5'-diphenylhexahydrofuro[3,4:3',4']furans. N. B. Galstukhova and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Sci.-Research Inst., Moscow). *Zhur. Obshchei Khim.* 27, 1857–65(1957). To 3.25 g. $LiAlH_4$ in 320 ml. Et_2O was added at 0° 8.7 g. $(BzCHCO_2Et)_2$ (m. 128–9°) in Et_2O and after 2 hrs. at 20° and 1 hr. at reflux the mixt. was treated with H_2O and dil. H_2SO_4 yielding 50.4% *meso-2,3-bis(α-hydroxybenzyl)-1,4-butanediol* (I), m. 137–8.5° ($ClCH_2CH_2Cl$); *tetraacetate*, m. 112–13° (EtOH); *tetrabenzoate*, m. 258–9° (dioxane). Similar reduction of the isomer of $(BzCHCO_2Et)_2$, m. 74–8°, gave *dl-2,3-bis(α-hydroxybenzyl)-1,4-butanediol* (II), m. 147.6–48° ($ClCH_2CH_2Cl$); *tetraacetate*, m. 143–3.5° (EtOH). Slow heating of 2.32 g. I with 2 g. $KHSO_4$ *in vacuo* to 110–70° 1 hr. followed by distn. gave 54% *2,5-diphenylhexahydrofuro[3,4:3',4']furan* (IIa), b_4 220–30°, m. 88.5–90° (abs. EtOH), which does not react with Br in $CHCl_3$ or with aq. $KMnO_4$. Similar treatment of II gave 25.6% *2,5'-diphenylhexahydrofuro[3,4:3',4']furan*, m. 72.5–4.5° (abs. EtOH). Hydrogenation of these in AcOH over Pd-C at room temp. and pressure gave, resp., 79% *3,4-dibenzyltetrahydrofuran*, m. 65.5–7°, and 49% *dl-2,3-dibenzyl-1,4-butanediol*, m. 87–8°. Reduction of *dl*-dibenzylsuccinic acid (III) with $LiAlH_4$ in Et_2O gave 18.3% *dl-dibenzyl-1,4-butanediol*, m. 87–8°, identical with above described. III with EtOH-H_2SO_4 gave 70.9% *di-Et ester*, m. 80–1.5°, which treated with $LiAlH_4$ gave 44.6% *dl-2,3-dibenzyl-1,4-butanediol*, m. 87–8°, identical with above described. The diol forms a *diacetate*, m. 73.5–4.5° (EtOH). Nitration of IIa with HNO_3 (d. 1.5) in AcOH at 20° gave a *2,5-bis(nitrophenyl)hexahydrofuro[3,4:3',4']furan*, m. 156.5–7.5° (EtOH). Successful nitration of the 2,5'-diphenyl analog of IIa could not be accomplished. Thus, Knorr's $(BzCHCO_2Et)_2$, m. 128–30°, is the *meso* isomer, while the so-called γ-isomer, m. 74–8°, is a racemate. G. M. K.

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Shchukina, M.N.

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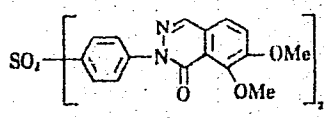
Some derivatives of 4,4'-dihydrazinodiphenyl sulfone and 4-hydrazinophenyl 2-acetamido-5-thiazolyl sulfone. T. V. Gortinskaya, V. G. Samolovova, and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 27, 1960–4(1957).—Heating 1.4 g. opianic acid in 50 ml. EtOH with 1 g. (p-HCl.H_2-$NNHC_6H_4$)$_2SO_2$ in 10 ml. H_2O gave a ppt. of 2.2 g. [4-{2,3,-4-$HO_2C(MeO)_2C_6H_2CH$:NNH}C_6H_4]$_2SO_2$ (I), m. 268–9°. If the reaction is run in H_2O there is formed yellow II, m. 258–60°, which changes to I on heating with ROH or alc. H_2SO_4. Hydrogenation of 4-nitrophenyl-2-amino-5-thiazolyl



(II)

sulfone in EtOH over Raney Ni gave 87% 4-$H_2NC_6H_4$ *analog*, m. 217–19°. Hydrogenation of 4-nitrophenyl-2-acetamido-5-thiazolyl sulfone over Raney Ni in H_2O gave the 4-$H_2NC_6H_4$ *analog*, m. 208–9°. This (5.4 g.), 42 ml. AcOH, 21 ml. concd. HCl, and 10.5 ml. H_2O diazotized with 1.1 g. $NaNO_2$ at 0° and the soln. treated with 7.85 g. $SnCl_2$ in 38.5 ml. HCl, and kept 2 days at room temp. gave 0.3 g. p-H_2NNH-C_6H_4 *analog HCl salt*, m. 222°; the filtrate treated with H_2S and filtered gave with NH_4OH 1.6 g. free *base* (IIA), m. 243–6°. The following *hydrazones* are reported: from

Gortinskaya, T.V.; Samoilovova, V.G.; Snchukina, M.N.

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(p-$H_2NNHC_6H_4$)$_2SO_2$ (III) and p-HOC_6H_4CHO, m. 238–40°; from III and p-$AcNHC_6H_4CHO$, m. 262–5°; from III and 3,4-$MeO(HO)C_6H_3CHO$, m. 250–2°; from *4-hydrazino-phenyl-2-acetamido-5-thiazolyl sulfone* (IV) and p-$AcNHC_6H_4CHO$, m. 221–3°; from IV and 3,4-$MeO(HO)C_6H_3CHO$, m. 238–40°; from IV and *opianic acid*, m. 263–4°. III showed some *in vitro* activity against human and avian tuberculosis and acid-fast saprophytic sp., *Microsporon* sp., *Trychophyton* sp., *Achorion* sp., and *actinomyces* sp. Some activity was found for III hydruzone, p-HOC_6H_4CHO, and IIA.

G. M. Kosolapoff.

SHCHUKINA, M. N.

Distr: 4E4j 7

Synthesis of some derivatives of β-phenylcysteine. T. P. Sycheva, I. V. Lebedeva, T. Kh. Trunn, and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchei Khim.* 27, 2287–92(1957); cf. Brown, *et al.*, *C.A.* 49, 0693b.—Passage of HCl into soln. of *phenylcysteine-HCl* (I) in abs. EtOH gave the *Et ester*, m. 140–50°. This with Ph_3CCl in $CHCl_3$ gave the *Et ester* of *N-tritylphenylcysteine*, m. 154–6° (EtOH). I treated dropwise to neutral reaction with 18% NaOH gave after air blowing 1 hr. *diphenylcystine*, decomp. 205–6°. Air blowing of soln. of I Et ester gave *diphenylcystine Et ester-2HCl*, decomp. 191°, which with BzCl gave *Et ester* of *N,N'-dibenzoyldiphenylcystine*, m. 147–9°. To 3 g. phenylserine Me ester-HCl and 30 ml. AcCl was added slowly 4.5 g. PCl_5 and after shaking 1 hr. the mixt. was chilled overnight yielding 0.6 g. *β-chlorophenylalanine Me ester-HCl*, decomp. 177° (EtOH-Et_2O). *p*-Nitrophenylserine Et ester-HCl with BzCl and Na_2CO_3 gave *N-benzoyl-p-nitrophenylserine Et ester*, m. 158–9°. Heating 5 g. *N*-benzoylphenylserine Et ester with 1.4 g. P_2S_5 to 110° 1.5 hrs. gave after 8 hrs. at 130° a mass which treated with EtOH, then with H_2O and extd. with Et_2O gave an oil which refluxed 7 hrs. with concd. HCl gave a low yield of $C_{16}H_{15}O_2NS.HCl$, m. 165–6°, which treated with *N* NaOH, and rapidly acidified with AcOH gave *2,5-diphenyl-4-thiasolinecarboxylic acid*, m. 140°. Phenylserine Me ester-HCl and Et_3N in $CHCl_3$ at 0°, followed by Ph_3CCl gave after 1.5 days at room temp. *N-tritylphenylserine Me ester*, m. 136–8°. To 30 ml. liquid

F. P. SYCHEVA, I. V. LEBEDEVA, ...

NH_3, 2.56 g. I, and 1.23 g. diphenylcystine was added at −40° 0.9 g. Na, followed by 1.5 ml. MeI and after 2 hrs. the mixt. yielded 2.5 g. *S-methylphenylcysteine*, m. 158–9°; *HCl salt*, m. 165–6°. Similar use of EtBr gave *S-ethylphenylcysteine-HCl*, m. 168–70°; the *free amino acid*, m. 153–4°. Similarly was prepd. *S-butylphenylcysteine*, m. 157–9°; *HCl salt*, m. 155–7°. Attempts to prep. phenylcysteine from chlorocinnamic acid and $CS(NH_2)_2$ failed.

G. M. Kosolapoff

SHCHUKINA, M.N.; GALSTUKHOVA, N.B.

Letter to the editor. Zhur.ob.khim. 27 no.10:2908 O '57. (MIRA 11:4)

(Nitration) (Furan)

79-1-48/63

AUTHORS: Yashunskiy, V. G., Shchukina, M. N.

TITLE: Compounds With Complex-Forming Properties (Veshchestva s kompleksoobrazuyushchey sposobnost'yu) I. Synthesis and Structure of "Complexon IV", i.e. 1,2-Diaminocyclohexane--N,N,N',N'-Tetraacetic Acid (I. Sintez i struktura "Kompleksona - IV" - 1,2-diaminotsiklogeksan-N,N,N',N'-tetrauksusnoy kisloty)

PERIODICAL: Zhurnal Obshchey Khimii, 1958, Vol.28, Nr 1, pp.230-234(USSR)

ABSTRACT: The methods described in publications (references 4, 5, 6) are little applicable to the synthesis of 1,2-diaminocyclohexane-N,N,N',N'-tetraacetic acid (formula I), because they give small yields. The authors worked out a more convenient synthesis of this compound by starting from the accessible dimethyl-(or diethyl-)-phthalate. They used Wieland's papers (reference 4) according to which this compound is synthesized from the dihydrazide of cyclohexane-dicarboxylic acid-1,2 (III) according to Curtius. According to the suggested scheme

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79-1-48/63

Compounds With Complex-Forming Properties. I. Synthesis and Structure of "Complexon IV", i.e. 1,2-Diaminocyclohexane-N,N,N',N'-Tetraacetic Acid

the synthesis of "complexon IV" is performed in four stages (the reaction process is given in formulae). The hydrogenation of dimethylphthalate takes place over a nickel catalyst below 50 - 10 atm. at 110 - 140°C without a solvent. On several hours heating the compound (III) is obtained from the hexahydroester with an excess of hydrazine-hydrate. Compound (III) is according to Curtius converted to the dichlorohydrate of 1,2-diaminocyclohexane (II). The final product (I) then results by the influence of monochloroacetic acid upon the dichlorohydrate of diamine in the presence of alkali and in all aspects corresponds to "complexon - IV" described in publications. The authors finally succeeded in proving that this "complexon IV" disposes of a trans- and not a cis-trans-figuration as several scientists had maintained. There are 2 tables, and 9 references, 2 of which are Slavic.

SUBMITTED: December 19, 1956

AVAILABLE: Library of Congress

Card 2/2 1. Chemistry 2. Cyclic compounds-Synthesis

SOV/79-28-7-18/64

AUTHORS: Markova, Yu. V., Zenkova, L. N., Shchukina, M. N.

TITLE: The Synthesis of Mercapto Amino Compounds(Sintez merkaptoamino-soyedineniy) III. The Synthesis of 3-Mercapto-4-Amino-2-Methyl-butane and of 5-Amino-1-Mercapto Pentane (III. Sintez 3-merkapto-4-amino-2-metilbutana i 5-amino-1-merkaptopentana)

PERIODICAL: Zhurnal obshchey khimii, 1958, Vol 28, Nr 7, pp 1811 - 1815 (USSR)

ABSTRACT: The homologs of β-mercapto ethylamine of the type R-CH(SH)-CH_2 have hitherto been little described. For this reason it was of interest to the authors to investigate the influence exerted by the length and the character of the alkyl chain as well as the positions of the functional groups, and to synthetize a number of these compounds. They synthetized for the first time the chlorine hydrate of 3-mercapto-4-amino-2-methylbutane, the chlorine hydrate of 5-amino-1-mercapto pentane and its acetyl derivative (see schemes 1 and 2). Already after this work had been completed a paper was published (Ref 3) by Langendorf in which the problems of interest to the authors of the present

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paper were explained to some extent. In the present paper it was shown that in the hydrolysis of N-benzoyl-5-amino-1-mercapto pentane with hydrochloric acid a partial oxidation of this compound into the corresponding disulfide takes place beside the formation of the chlorine hydrate of 5-amino-1-mercapto pentane. As final product of the oxidation hydrolysis of the chlorine hydrate of N-benzoyl-5-amino-1-isothiuronium pentane the dichlorine hydrate of 5-amino-1-isothiuronium pentane was obtained which did not further hydrolize when heated with alkali liquor. In the oxidation of N-benzoyl-5-amino-1-mercapto pentane with an iodine alcohol solution a bis(N-benzoyl-5-aminopentyl)-disulfide was obtained. A convenient synthesis of N-benzoyl-5-amino-1-chloro pentane (in a yield of 63%) was elaborated. There are 10 references, 1 of which is Soviet.

The Synthesis of Mercapto Amino Compounds. III. The Synthesis of 3-Mercapto-4-Amino-2-Methylbutane and of 5-Amino-1-Mercapto Pentane

SOV/79-28-7-18/64

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze (All-Union Institute of Scientific Chemical and Pharmaceutical Research imeni S. Ordzhonikidze)

SUBMITTED: June 27, 1957

1. Butanethiols--Synthesis 2. Pentanethiols--Synthesis

Card 3/3

SHCHUKINA, M.N., prof.; MASHKOVSKIY, M.D., prof.; PERSHIN, G.N., prof., laureat Stalinskoy premii, otv.red.; SERGIYEVSKAYA, S.I., prof., red.; MAGIDSON, O.Yu., prof., laureat Stalinskoy premii, red.; UTKIN, L.M., prof., red.; GROZDEVA, Ye.I., red.; LYUDKOVSKAYA, N.I., tekhn.red.

[Chemistry and medicine] Khimiia i meditsina. Otv.red. G.N. Pershin. Moskva, Medgiz. No.9. [Aminazine] Aminazin. 1959. 241 p. (MIRA 12:6)

1. Moscow. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut. 2. Zaveduyushchaya laboratoriyey protivotuberkuleznykh soyedineniy Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta imeni S.Ordzhonikidze (for Shchukina). 3. Zaveduyushchiy laboratoriyey otdela farmakologii Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta imeni S.Ordzhonikidze (for Mashkovskiy).

(CHLORPROMAZINE)

SHCHUKINA, M.N., prof.

Preface. Khim.i med. no.11:3-5 '59. (MIRA 13:6)
(RADIOACTIVE TRACERS)

MAYMIND, V.I.; ZHUKOVA, T.F.; KOSOLAPOVA, N.A.; SHCHUKINA, M.N.

Synthesis of S^{35}-methionine. Khim.i med. no.11:9-14 '59.
(MIRA 13:6)

(METHIONINE)

POZHARSKAYA, A.M.; ZHUKOVA, T.F.; SHCHUKINA, M.N.

Synthesis of D-cysteine-S^{35}. Khim.i med. no.11:14-17 '59.
(MIRA 13:6)

(CYSTEINE)

MARKOVA, Yu.V.; ZHUKOVA, T.F.; SHCHUKINA, M.N.

Synthesis of S^{35}-carbon disulfide. Khim.i med. no.11:26-29 '59. (MIRA 13:6)

(CARBON DISULPHIDE)

MARKOVA, Yu.V.; ZENKOVA, L.N.; SHCHUKINA, M.N.

Synthesis of S^{35}-thiamine. Khim.i med. no.11:29-34 '59.
(MIRA 13:6)

(THIAMINE)

PREDVODITELEVA, G.S.; SHCHUKINA, M.M.

Synthesis of S^{35}-aminazine. Khim. i med. no.11:34-39 '59.
(MIRA 13:6)

(CHLORPROMAZINE)

MARKOVA, Yu.V.; KUZ'MINA, K.K.; SHCHUKINA, M.N.

Synthesis of S^{35}-merkamin. Khim.i med. no.11:39-42 '59.
(MIRA 13:6)

(ETHANETHIOL)

MAHKOVA, Yu.V.; ZENKOVA, L.N.; SHCHUKINA, M.N.

New method for the synthesis of C^{14}-paraaminobenzoic acid and obtaining C^{14}-anesthesin, novocaine, and cocaine. Khim.i med. no.11:53-59 '59. (MIRA 13:6)
(BENZOIC ACID) (ANESTHETICS)

MARKOVA, Yu.V.; ZENKOVA, L.N.; SHCHUKINA, M.N.

Synthesis of barbiturates labeled with C^{14} and S^{35}. Khim.i med. no.11:60-68 '59. (MIRA 13:6)

(BARBITURATES)

SYCHEVA, T.P.; LEBEDEVA, I.V.; SHCHUKINA, M.N.

Model synthesis of C^{14}-dimedrol. Khim.i med. no.11:77-82 '59.
(MIRA 13:6)

(DIPHENHYDRAMINE)

SAMOLOVOVA, V.G.; YERMOLAYEVA, V.G.; GORTINSKAYA, T.V.; YASHUNSKIY, V.G.; SHCHUKINA, M.N.

Synthesis of asterol and other derivatives of aminotoxibenzthiazoles. Med. prom. 13 no.5:23-26 My '59. (MIRA 12:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(THIAZOLE)

PREDVODITELEVA, G.S.; SHCHUKINA, M.N.

New variant of diacarb synthesis. Med.prom. 13 no.9:24-26 S '59.
(MIRA 13:1)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(THIADIAZOLE SULFONAMIDE)

3 (4)

AUTHORS: Chao Erh-chang, Mchukina, M. N. SOV/79-29-3-56/61

TITLE: Synthesis of the Dialkyl-amino-alkyl-derivatives of Indazol (Sintez dialkilaminoalkil'nykh proizvodnykh indazola)

PERIODICAL: Zhurnal obshchey khimii, 1959, Vol 29, Nr 3, pp 1012-1020 (USSR)

ABSTRACT: The authors carried out the synthesis of the above mentioned compounds in order to investigate their chemical, pharmacological, and antibacterial properties since the dialkyl-amino-alkyl grouping plays an important role in the pharmaceutical products. Many synthetic spasmolitic anaesthetic antimalaria remedy and others contain this grouping which is connected with a nitrogen- or oxygen atom. For this reason it was interesting to synthesize compounds of such a type in the series of indazol (which is according to its structure assumed to be an isostere of indol and an isomer of benzimidazole) which are as heterocycles ingredients of the biologically important products. The N-diethyl-amino-ethyl-6-nitroindazol was synthesized with a good yield by the condensation of the 6-nitro-indazol with diethyl-amino-ethylchloride in the presence of sodium alcoholate. The N-dimethyl-amino-ethyl-6-nitroindazol, N-dimethyl-amino-ethyl-3-chloroindazol and N-dimethyl-amino-

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ethyl-indazol were obtained by the same method. Since the free base of dimethyl-amino-ethyl chloride polymerizes easily in the case of distillation its hydrochloride and the double quantity of alcoholate were introduced into the reaction. In the case of the indazol the yield is smaller than in the case of 6-nitro- and 3-chloroindazol which may be explained by the presence of chlorine and the nitrogroup which draws off the electrons. This increases the activity of the hydrogen atom at the nitrogen (Scheme). In the case of the alkylation of indazol and its derivatives (Ref 1), as well as in the case of its condensation with dialkyl-amino-alkyl chlorides 1- and 2-derivatives are formed. Thus the 1- and 2-diethyl-amino-ethyl- and dimethyl-amino-ethyl derivatives of the 6-nitroindazol, 6-aminoindazol and 3-chloro-6-nitroindazol, the 1- and 2-dimethyl-amino-ethyl indazols, and the 1- and 2-dimethyl-amino-ethyl-3-chloroindazols as well as the 2-diethyl-amino-ethyl-6-oxyindazol were obtained. The separation of the mixtures of the 1- and 2-isomers was obtained by fractionated crystallization of the hydrochlorides or by the fractionated precipitation of the picrates. The structure was proved by comparison with the spectral analysis. There are 4 figures and 10 references.

SOV/79-29-3-56/61

Synthesis of the Dialkyl-amino-alkyl-derivatives of Indazol

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevtiches-kiy institut (All-Union Scientific Research Institute of Chemical Pharmacy)

SUBMITTED: January 8, 1958

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5(3) SOV/79-29-8-59/81

AUTHORS: Yashunskiy, V. G., Vasil'yeva, V. P., Tikhonova, L. I., Shchukina, M. N.

TITLE: Substances With a Complex-forming Capacity. IV. Trans-1,2-diaminocyclohexene- and 1-Phenylethylenediamine-N,N,N',N'-tetraacetic Acids

PERIODICAL: Zhurnal obshchey khimii, 1959, Vol 29, Nr 8, pp 2709 - 2712 (USSR)

ABSTRACT: The authors previously reported on the synthesis and investigation of the complex-forming capacities of some alicyclic 1,2-diaminetetraacetic acids of a trans-configuration (Refs 1,2). In order to complement this series the compound (I) was synthesized. The initial product for the synthesis of this compound was the dimethyl ester of the cis-cyclohexene-(4)-dicarboxylic acid-1,2 obtained by the condensation of butadiene with the anhydride of maleic acid. When this cis-diester is heated with hydrazine hydrate without solvent the trans-dihydrazide forms (Ref 1). The latter was transformed according to Curtius into the dichlorohydrate of the hitherto

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unknown trans-1,2-diaminocyclohexene-(4) which was treated with an excess of chloroacetic acid in an alkaline medium which led to the compound (I). In order to investigate the influence of the substitutes on the complex-forming capacity of the complexons of the ethylenediaminetetraacetic acid series the compound (II) obtained from 1,2-diaminoethylbenzene by two different methods was synthesized (Ref 3, and Rodionov, Ref 4). The tetraacetic acid could only be synthesized by heating 1,2-diaminoethylbenzene with an excess of bromoacetic acid in the presence of caustic soda at 40°. Thus two compounds hitherto not described were synthesized: trans-1,2-diamino-cyclohexene-(4)-, and 1-phenylethylenediaminetetraacetic acid. The complex-forming capacity of the synthesized compounds was determined chromatographically (Ref 5) by way of comparison with ethylenediaminetetraacetic acid. By this method it was shown that the new complexons have a complex-forming capacity of the same order as ethylenediaminetetraacetic acid. The table shows the result of these chromatographic determinations.

Substances With a Complex-forming Capacity. IV. Trans-1,2-diaminocyclohexene- and 1-Phenylethylenediamine-N,N,N',N'-tetra-acetic Acids

SOV/79-29-8-59/81

The results of the investigation of complexon (II) show that the presence of the phenyl radical beside one of the amino groups of ethylenediaminetetraacetic acid has but little effect upon the complex-forming capacity. There are 1 table and 6 references, 5 of which are Soviet.

SUBMITTED: July 5, 1958

Card 3/3

5 (3)

AUTHORS: Murav'yeva, K. M., Shchukina, M. N. SOV/20-126-6-36/67

TITLE: Synthesis and Regroupings in the Series of Thiazoline Imine (Sintez i peregruppirovki v ryadu tiazolinimina)

PERIODICAL: Doklady Akademii nauk SSSR, 1959, Vol 126, Nr 6, pp 1274 - 1277 (USSR)

ABSTRACT: In the condensation of thiourea or of its substituents with α-halogen carbonyl compounds derivatives of the 2-amino-thiazole or thiazoline imine are formed. In the present paper the authors investigated the condensation of the α-halogen ketones with symmetric diaryl and aryl-acyl urea as well as the regroupings of the cyclic compounds obtained. It was found that the reaction course depends on the presence of the hydrogen ions in the reaction medium. If the forming halogen hydrogen is linked by triethylamine, 4-oxy-thiazolidine derivatives are formed. In aqueous or alcoholic HCl solution they cleave-off water. The intermediate compounds are unstable especially if they were produced from diaryl thiourea (Table 1, I a). In the condensation of the symmetric ditolyl and diphenetidyl-thiourea with acetone chloride the authors directly obtained 2-tolyl-imino-3-tolyl-4-methyl-thiazoline (II) and 2-p-ethoxy-phenyl-

-imino-3-p-ethoxy-phenyl-4-methyl-thiazoline (III) whithout intermediate compounds. Intermediate products in the condensation of the α-halogen ketones with N-aryl-N'-acyl-thiourea show a stronger stability. They cleave-off water in the action of HCl in the cold, and pass over into the corresponding thiazoline compounds, which in most cases strongly differ by their melting temperature (IV-IX). The acyl-imino-thiazolines (IV, V, VI) produced by the authors are saponified with HCl by a short heating into 2-imino-3-phenyl-4-methyl-thiazoline (Ref 5). By boiling this imine (or IV, V, VI) for several hours with HCl a regrouping and a formation of 2-phenyl-amino-4-methyl-thiazole (Ref 6) take place. The compound VII was saponified to a 2-imino-3,4-diphenyl-thiazoline (Ref 5). After a long boiling with HCl this imine showed a regrouping and yielded 2-phenyl-amino-4-phenyl--thiazole (Refs 5,7). In the heating of ω-bromo acetophenone and phenyl acetyl thiourea in an absolute alcoholic solution, 2-acetyl-imino-3,4-diphenyl-thiazoline-4 was produced (VIII). This compound is saponified into 2-imino-3,4-diphenyl-thiazoline-4. However, ω-bromo acetophenone as well as phenyl acetyl thiourea form the oxy compound IVa. Thus in the reaction course

benzoyl as if from the methylene group migrates to the nitrogen of the thiourea, while acetyl migrates from this nitrogen atom to the methylene group. The compounds IX, X and XI are saponified to 2-imino-3-phenyl-4,5,6,7-tetra-hydro-benzthiazoline (XII) in heating with 20% HCl. This substance is transformed into 2-phenyl-amino-4,5,6,7-tetra-hydro-benzthiazole (Ref 8) by boiling during several days with 20% HCl. The authors explain the above transformations by the following: The thiourea substituents enter in their isoform the reaction with α-halogen ketones by forming S-β-keto-substituents of the isothioureas. They are still subject to further transformations. The carbonyl oxygen captures a proton from the aminophenyl residue which brings about a formation of an N-C-bond. 4-oxy-thiazolidine compounds are formed which readily cleave-off water. The regrouping of the 2-imino-3,4-substituents of thiazoline in boiling with HCl may be explained by the addition of a proton to the nitrogen of the ring, by the rupture of the 3,4-bond and by the resulting polarization of the molecule. The cycle is then closed at the nitrogen of the imino group and 2-phenyl-amino-4-substituted thiazoles are formed. The reactions investigated show that

Synthesis and Regroupings in the Series of Thiazoline Imine SOV/20-126-6-36/67

the condensation of the α-halogen ketones with N-phenyl-N'--acyl-thiourea passes over the stage of the 4-oxy-thiazolidine derivatives. These compounds are, similar to the 2-imino-thiazolines-4, very unstable and have the tendency towards regroupings which bring about the rupture of the heterocycle. There are 1 table and 8 references, 2 of which are Soviet.

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonikidze (All-Union Scientific Chemo--pharmaceutical Research Institute imeni S. Ordzhonikidze)

PRESENTED: February 24, 1959, by I. L. Knunyants, Academician

SUBMITTED: February 19, 1959

Card 4/4

RUBTSOV, M.V., prof., otv. red.; PERSHIN, G.N., prof., zam. otv. red.; MAGIDSON, O.Yu., prof., red.; MASHKOVSKIY, M.D., prof., red.; UTKIN, L.M., prof., red.; RUZHENTSEVA, A.K., prof., red.; SHCHUKINA, M.N., prof., red.; BAYCHIKOV, A.G., kand. tekhn. nauk, red.; MIKHALEV, V.A., kand. khim. nauk, red.; RYAZANTSEV, M.D., kand. tekhn. nauk, red.; SUVOROV, N.N., kand. khim. nauk, red.; ILYASHKEVICH, A.M., st. nauchnyy sotr., red.

[Basic trends in the work of the S.Ordzhonikidze All-Union Chemico-pharmaceutical Scientific Research Institute; survey of its activity from 1920 to 1957] Osnovnye napravleniia rabot VNIKhFI; obzor deiatel'nosti za 1920-1957 gg. Moskva, 1959. 649 p. (MIRA 15:5)

1. Moscow. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut.
(CHEMISTRY, MEDICAL AND PHARMACEUTICAL)

SYCHEVA, T.P.; LEBEDEVA, I.V.; SHCHUKINA, M.N.

Reaction of α-methylthiazole with sulfur and amines. Zhur. VKHO 5 no. 2:234-235 '60. (MIRA 14:2)

1. Nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imen Sergo Ordzhonikidze.
(Thiazole) (Sulfur) (Amines)

SYCHEVA, T.P.; KUZ'MICHEVA, T.P.; CHERNYAYEVA, A.T.; TRUPP, T.Kh.; SHCHUKINA, M.N.

Synthesis of apressin. Med.prom. 14 no.2:13-17 F '60. (MIRA 13:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(PHTHALAZINE)

GALSTUKHOVA, N.B.; SHCHUKINA, M.N.

Synthesis of etoxide, a new antituberculosis drug. Med. prom. 14 no.8:15-18 Ag '60. (MIRA 13:8)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonididze.
(CARBANILIDE)

GORTINSKAYA, T.V.; SHEINA, N.P.; SHCHUKINA, M.N.

Determination of the dissolution properties and the mechanical hardness of tablets. Materials for the 9th edition of the State Pharmacopoeia of the U.S.S.R. Med. prom. 14 no.9:15-23 S '60. (MIRA 13:9)
(TABLETS (MEDICINE))
(DRUG INDUSTRY--EQUIPMENT AND SUPPLIES)

GORTINSKAYA, T.V.; SHEINA, N.P.; SHCHUKINA, M.N.

Some derivatives of 3-methoxy-6-(sulfanilamido)-pyridazine. Med. prom. 14 no.9:23-25 S '60. (MIRA 13:9)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(PYRIDAZINE)

SHCHUKINA, M.N.

Synthetic drugs produced by a number of French pharmaceutical firms. Med. prom. 14 no. 10:57-62 O '60. (MIRA 13:10)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(FRANCE--DRUGS)

ZHEREBCHENKO, P.G.; GOLOVCHINSKAYA, Ye.S.; KOSTYANOVSKIY, R.G.; KRASNYKH, I.G.; KUZNETS, Ye.I.; MAGIDSON, O.Yu.; MURASHOVA, V.S.; PASTUKHOVA, I.S.; PREOBRAZHENSKAYA, M.N.; SUVOROV, N.N.; TER-VARTANYAN, L.S.; ZHKHINVADZE, K.A.; SHASHKOV, V.S.; SHCHUKINA, M.N.

Role of oxidative deamination in the mechanism of radiation protection afforded by some amines. Zhur.ob.biol. 21 no.2: 157-160 Mr-Ap '60. (MIRA 13:6)

(RADIATION PROTECTION) (DEAMINATION)

AUTHORS: [illegible]

TITLE: Some Phthalazine Derivatives With Potential Chemotherapeutic Activity

PERIODICAL: Zhurnal obshchey khimii, 1960, Vol 30, No 3, pp 809-811 (USSR)

ABSTRACT: This article deals with some phthalazine derivatives assumed to be effective against the tuberculosis bacillus. 1-Benzoyloxy-3-phenyl-4-phthalazone and its analogs with nitro-, amino-, and acetamino groups in para position on the phenyl radical, were synthesized by the authors to investigate their therapeutic activity. Phenyl- and p-nitrophenylhydrazines with phthalic anhydride yielded the corresponding 1,4-diketo-3-arylotetrahydrophthalazines which were subsequently alkylated. Catalytic hydrogenation of 1-benzoyloxy-3-(p-nitrophenyl)-phthalazone gave the corresponding amine, which was converted into its acetyl derivative. Since 1-hydroxyphthalazine is

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[illegible]

[illegible] tuberculostatic activity

SOV/[illegible]-58-[illegible]-25/25

[illegible] therapeutic action, the hydrazones with such active antituberculous compounds as rimifon, p-aminosalicylaldehyde, and p-dimethylaminobenzaldehyde were synthesized. Some derivatives of the phthalazone carboxylic acid were also obtained. None of the synthesized compounds, with the exception of 1-benzoyl-4-phenyl-6-phthalazone, showed any appreciable activity against tuberculosis bacilli. The last compound was tested on the tuberculosis strain $H_{37}Rv$, diluted 1 to 512,000 without serum, and 1 to 16,000 with serum. In experimental tuberculosis treatment of white mice, the compound was found to be totally inactive. Biological research was conducted under the supervision of G. N. Pershin at the chemotherapy department of the S. A. Vishkarev All-Union Chemical and Pharmaceutical Scientific Research Institute. There are 11 references, 4 Swiss, 3 U.K., 1 U.S., 1 French, 1 Soviet, 1 German. The U.S. and U.K. references are: E. Berlin, D. Drain, et al., J. Pharm. Pharmac., 1[illegible], 4, 11, 744; D. Drain, D. Seymour, J. Chem. Soc., 1955,

Card [illegible]

..., F. Rowe, J. Hiram, A. Peters, J. Chem. Soc., ..., ..., ..., M. ... F. Gregory, et al., Proc. Soc. Exp. Biol. Med., 79, 563 (1952).

ASSOCIATION: S. Ordzhonikidze All-Union Chemical and Pharmaceutical Scientific Research Institute (Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze)

SUBMITTED February 7, 1958

Card 1/1

5/3700

AUTHORS: Vasil'yeva, V. F., Yushunskiy, V. G., Shchukina, M. N.

TITLE: Letters to the Editor. Concerning the Reaction of Sydnones With Derivatives of α, β-Unsaturated Acids

PERIODICAL: Zhurnal obshchey khimii, 1960, Vol 30, Nr 2, p 658 (USSR)

ABSTRACT: Sydnones on heating with nitriles and esters of α, β-unsaturated acids undergo cleavage and yield derivatives of pyrazoline and pyrazole, accompanied by evolution of the carbon dioxide. While the reaction of sydnones with unsaturated esters yields esters of substituted pyrazoli-necarboxylic acids, the reaction of sydnones with nitriles yields only substituted pyrazoles. In both cases, probably, the formation of esters or nitriles of substituted pyrazolinecarboxylic acids takes place. However, the sydno group in these

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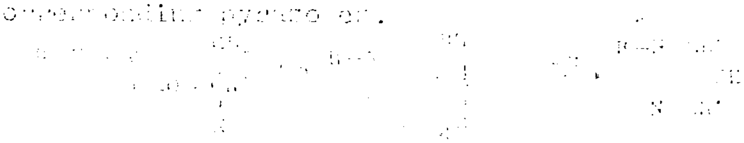
Letters to the Editor. [illegible] the Reaction of Sydnones With [illegible] of α, β-[illegible] Acids

[illegible]

compound is [illegible] by heating [illegible] the conversion of [illegible] into corresponding pyrazoles.



[illegible]

The [illegible] of derivatives of unsaturated [illegible] [illegible] that the [illegible]-carbon atom of ethylene bond is directed toward the carbon atom of sydnone, and [illegible] C-atom of the [illegible] bond, toward the unsubstituted nitrogen atom. Heating 3-phenylsydnone with excess acrylonitrile yields 1-phenylpyrazole (yield 60%). The structure of the obtained compounds was confirmed by spectral analysis, as well as by comparison with literature data. There is 1 German reference.

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APPROVED FOR RELEASE: 08/23/2000 CIA-RDP86-00513R001548920018-3"

Letters to the Editor. Concerning the Reaction of Sydnones With Derivatives of α, β-Unsaturated Acids

77934
SOV/79-30-1-79/[illegible]

ASSOCIATION: S. Ordzhonikidze All-Union Scientific Research Chemical and Pharmaceutical Institute (Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze)

SUBMITTED: October 26, 1959

Card 1/1

79307
SOV/79-30-3-61/69

AUTHORS: Markova, Yu. V., Kuz'mina, K. K., Shchukina, M. N.

TITLE: Synthesis of Mercaptoamino Compounds. IV. Synthesis of β-Mercaptoethylamine and 1-Amino-2-mercaptobutane

PERIODICAL: Zhurnal obshchey khimii, 1960, Vol 30, Nr 3, pp 1039-1043 (USSR)

ABSTRACT: This paper describes synthesis of β-mercaptoethylamine and 1-amino-2-mercaptobutane according to the scheme used previously for synthesis of 3-mercapto-4-amino-2-methylbutane (Yu. V. Markova, L. N. Zenkova, M. N. Shchukina, ZhOKh, 28, 1811 (1958)):

$$RCHOHCH_2NH_2 \cdot HCl \xrightarrow{SOCl_2} RCHClCH_2NH_2 \cdot HCl \xrightarrow[NaOH]{CS_2} RCH(S)-CH_2(N)-C(=S)-SH \longrightarrow$$

$$\xrightarrow{HCl} RCHSHCH_2NH_2 \cdot HCl$$

R = H, C_2H_5.

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Synthesis of Mercaptoamino Compounds. IV

78307
SOV/79-30-3-61/69

β-Mercaptoethylamine hydrochloride (I) was obtained (48%, based on the initial ethylamine) as follows: a mixture of 2-mercaptothiazoline and HCl (20% solution) was boiled for 50 hours on an oil bath; the mixture was evaporated under vacuum and dissolved in absolute alcohol; the alcoholic solution, to which charcoal had been added, was warmed and filtered; absolute ether was added to the filtrate and left to stand for 24 hr.

The precipitate was removed by filtration. I has mp 67-69°; 2-mercapto-1-aminobutane hydrochloride (II) was obtained (50%) by the same method as I; it has mp 134-138°. There are 10 references, 1 U.S., 5 German, 2 Swiss, 2 Soviet. The U.S. reference is: R. H. Haal, F. Wright, J. Am. Chem. Soc., 73, 2215 (1951).

ASSOCIATION: S. Ordzhonekidze All-Union Chemical-Pharmaceutical Scientific Research Institute (Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze)

SUBMITTED: December 27, 1958

Card 2/2

SAMOLOVOVA, V.G.; GORTINSKAYA, T.V.; SHCHUKINA, M.N.

Phenoxazine. Part 1: Synthesis of some 10-substituted derivatives of phenoxazine. Zhur.ob.khim. 30 no.5:1516-1517 My '60. (MIRA 13:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Phenoxazine)

GORSHINSKAYA, T.V.; SHCHUKINA, M.N.

Some derivatives of pyridazine. Zhur.ob.khim. 30 no.5: 1518-1520 My '60. (MIRA 13:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Pyridazine)

PREDVODITELEVA, G.S.; SHCHUKINA, M.N.

Studies in the phenoxazine series. Part 2: Synthesis of some derivatives of substituted 1-phenoxazinecarboxylic acid. Zhur.ob.khim. 30 no.6:1893-1897 Je '60. (MIRA 13:6)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(Phenoxazine) (Phenoxazinecarboxylic acid)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series. Part 1: Condensation of chloroacetone and -chlorocyclohexanone with sym. diaryl- and arylacylthioureas. Zhur.ob. khim. 30 no.7:2327-2334 Jl '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Acetone) (Cyclohexanone) (Urea)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series. Part 2: Condensation of ω-bromoacetophenone with N-phenyl-N'-acylthioureas. Zhur.ob.khim. 30 no.7:2334-2340 Jl '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Urea) (Acetophenone)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series. Part 3: Rearrangement of 2-imino-3-phenyl-4-thiazolines into 2-phenylaminothiazoles. Zhur.ob.khim. 30 no.7:2340-2343 Jl '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Thiazoline) (Thiazole)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series. Part 4: Effect of acetylating agents on 2-acylimino-4-hydroxythiazolidines. Zhur.ob.khim. 30 no.7:2344-2348 Jl '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Thiazolidine)

BANASHEK, A.; SHCHUKINA, M.N.

β- And γ-pyridylthiazolines. Zhur.ob.khim. 30 no.10:3328-3332 O '61. (MIRA 14:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Thiazoline)

S/073/60/030/012/008/027
B001/B064

AUTHORS: Yashunskiy, V. G., Smolin, D. D., Yermolayeva, V. G., and Shchukina, M. N.

TITLE: Substances Capable of Complex Formation. V. 2,2'-Diamino-diethyl Ether-N,N,N',N'-tetraacetic Acid

PERIODICAL: Zhurnal obshchey khimii, 1960, Vol. 30, No. 12, pp. 3916-3918

TEXT: The authors continue their studies (Ref. 2) of the synthesis of complexons by synthesizing 2,2'-diamino-diethyl ether-tetraacetic acid; this synthesis has hitherto not been described. It may, however, be assumed that this complex was obtained on the basis of data of an English patent (Ref. 3) from 2,2'-diamino-diethyl ether by carboxymethylation. Several experiments had failed before the complex was obtained by reacting 2,2'-diamino-diethyl ether. The diamino ether was obtained from 2,2'-dichloro diethyl ether with the diphthalimide derivative by the reaction of Gabriel (Ref. 4), however, the 2,2'-di(phthalimido)-diethyl ether was split off by boiling with an alcohol solution of hydrazine hydrate and subsequent treatment with hydrochloric acid which simplified the reaction and led to an

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abruptly increasing yield. The diamine was separated as dichloro hydrate and reacted with monochloro acetic acid. The reaction was normal and took place in alkaline medium (Ref. 2). Since it was not possible to precipitate tetra acid by acidifying the reaction mass, which is the case with some other complexons, two methods of precipitation were applied. The cationite KU-2 was used for the first one applied in the study of Ref. 5. By the latter method the reaction mixture was acidified until the acid reaction toward Congo red as indicator had been reached and, after the separation of sodium chloride from the solution, the monosodium salt of the complexon precipitated with methanol and purified by repeated precipitation with methanol from water. There are 6 references: 2 Soviet, 1 US, 1 Swiss, 1 German, and 1 British.

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze (All-Union Chemical and Pharmaceutical Scientific Research Institute imeni S. Ordzhonikidze)

SUBMITTED: January 11, 1960

SYCHEVA, T.P.; SHCHUKINA, M.N.

Reaction of 2-methyloxazole with sulfur and amines. Zhur.VKHO 6 no.1:117-118 '61. (MIRA 14:3)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S.Ordzhonikidze.
(Oxazole) (Amines) (Sulfur)

SHCHUKINA, M.N.

Modern antituberculosis drugs. Med. prom. 15 no. 4:13-25 Ap '61.
(MIRA 14:4)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(TUBERCULOSIS—PREVENTION) (DRUGS)

YASHUNSKIY, V.G.; SHCHUKINA, M.N.; YERMOLAYEVA, V.G.; SAMOYLOVA, O.I.

Synthesis of imizine hydrochloride, N-(3-dimethylaminopropyl)-iminodibenzyl. Med. prom. 15 no.12:10-13 D '61. (MIRA 15:2)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(IMIPRAMINE)

SYCHEVA, T.P.; NEKHLIN, Ya.G.; SHCHUKINA, M.N.

Synthesis of phenizine. Med. prom. 15 no.12:14-17 D '61.
(MIRA 15:2)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(HYDRAZINE)